

University of Alberta

**Variation by Oncologist in Treatment Patterns of Adjuvant Chemotherapy  
for Colorectal Cancer and End-of-life Care for Colorectal Cancer Patients in  
Alberta, Canada**

by

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A thesis submitted to the Faculty of Graduate Studies and Research  
in partial fulfillment of the requirements for the degree of

Master of Science

in

Epidemiology

School of Public Health

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Fall 2012  
Edmonton, Alberta

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## **Dedication**

*In memory of my grandmother.*

## **Abstract**

Colorectal cancer is one of major public health concerns in Canada. Prior studies have demonstrated a substantial proportion of patients in Alberta with stage III colon or stage II/III rectal cancer did not receive guideline-recommended adjuvant chemotherapy. Certain patient factors related with not receiving adjuvant chemotherapy have been assessed. In this population-based study, we examined the relationship between oncologist and patients' not receiving adjuvant chemotherapy and estimated the oncologist-specific probability for patient's not receiving adjuvant chemotherapy.

End-of-life (EOL) care forms an important component in cancer care continuum. Using validated quality indicators for EOL cancer care, we evaluated aggressiveness of EOL care in Alberta for patients who died of colorectal cancer in 2006-2009 and examined factors that were related to aggressive use of health care services at the EOL.

## **Acknowledgment**

This thesis would not have been possible without the contribution of several people.

First and foremost, I owe my deepest gratitude to my supervisor, Dr. Yutaka Yasui, a respectful scholar and gentleman, who kindled the light in my study pursuit and built me up with great support over the past years. He is one of the best teachers I have ever met. I am also very grateful to my co-supervisor Dr. Marcy Winget, who provided me great opportunities to be engaged in cancer research and has been guiding me closely in my thesis project with tremendous effort and support. She enlightened me to think carefully and communicate effectively through her keen critical questions and advices. I have been fortunate to be guided by both supervisors. Their influence on my ways of learning is profound.

I am thankful to my external committee Dr. Jonathan White, our collaborator Dr. Chris deGara, as well as Dr. Yan Yuan for their generous availability and valuable insights on my thesis. I thank my instructors at the School of Public Health, for their endeavor to impart the best knowledge to me. My colleagues in Dr Yasui's research group and staff in Dr Winget's team are also highly appreciated, for their time and talents in assisting me during my program.

Finally, I have been blessed with a family that has always been a source of understanding and encouragement. I thank my parents, parents-in-law, my husband and my son, for their strong support and infinite love.

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## List of Symbols, Nomenclature, and Abbreviations

AJCC:	American Joint Committee on Cancer
CI:	Confidence Interval
CEA:	Carcinogenic Embryonic Antigen
CRC:	Colorectal Cancer
CT:	Computerized/Computed Tomography
ER:	Emergency Room
EMR:	Electronic Medical Record
EOL:	End-of-life
FOBT:	Fecal Occult Blood Test
FIT:	Fecal Immunochemical Test
ICU:	Intensive Care Unit
ICD-O:	International Classification of Diseases for Oncology
ICD-9-CM:	International Classification of Diseases, 9 <sup>th</sup> Revision, Clinical Modification
NIH:	National Institute of Health
OR:	Odds Ratio
MRI:	Magnetic Resonance Imaging
PET:	Positron Emission Tomography
TME:	Total Mesorectal Excision
TNM:	Tumor, Node, and Metastasis
U.S.:	United States
5-FU:	5-Fluorouracil

## Chapter 1 Introduction

This is a paper format thesis prepared in accordance with the guideline of the Faculty of Graduate Studies and Research, University of Alberta. The thesis is organized as follows:

**Chapter 1** The introductory chapter for the full thesis, providing background, objectives, and significance of the work

**Chapter 2** The first manuscript addressing the variation among oncologists in Alberta in their use of adjuvant chemotherapy for treatment of patients with stage II/III colorectal cancer<sup>1</sup>

**Chapter 3** The second manuscript that quantifies the patterns of health care use at the end of life among colorectal cancer patients in Alberta; and identifies the factors associated with disparities in use of care<sup>2</sup>

**Chapter 4** The concluding chapter that summarizes the findings, their implications, and future directions of research

Each chapter is presented with its own set of references.

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<sup>1</sup> A version of this chapter has been submitted for publication in March 2012.

<sup>2</sup> The manuscript for this chapter has been written with the intent to submit for publication.

## **1.1 Preamble**

This thesis is a sub-project of a larger research project, conducted by Cancer Care, Alberta Health Services, under the leadership of Dr. Marcy Winget. The overall objective of the research project is to develop a framework for identifying major colorectal cancer (CRC) care trajectories that can be implemented to enable routine evaluation of patient care, thereby, to identify the priority areas for system improvement. Data sources include Alberta Cancer Registry, Cancer Care electronic medical record, hospital administrative data, physician billing, medical charts, and Canadian census data.

By linking various data sources, previous projects have evaluated 1) adherence to longstanding guidelines for treatment of patients with stage III colon<sup>1</sup> and stage II/III rectal cancer,<sup>2</sup> including identification of clinical/demographic disparities; 2) the association between timing of adjuvant chemotherapy and survival in stage III colon<sup>3</sup> and stage II/III rectal cancer patients.<sup>4</sup>

Following these studies, this thesis aims to: 1) examine system-related disparity, specifically, disparity among oncologists, in receipt of guideline-recommended adjuvant chemotherapy for patients with stage III colon and stage II/III rectal cancer; and 2) evaluate aggressiveness of health care use at the end-of-life (EOL) for patients who died of CRC.

## **1.2 Background**

CRC is the third most common cancer diagnosis and the second leading cause of cancer death in Canada. According to statistics provided by the Canadian Cancer Society in 2011, one in 13

Canadian males and one in 16 Canadian females will be diagnosed with CRC in their life time; half of them are expected to die from it; the annual incidence of CRC is 22,000 and mortality is 8,900 (12% of all cancer deaths).<sup>5</sup>

More than 95% of CRC refers to a type of cancer known as adenocarcinoma. Treatment for colorectal adenocarcinoma is primarily determined by the stage of cancer, which describes the extent the cancer has spread in the body. The stage takes into account the size of a tumor, how deeply it has penetrated, whether it has invaded adjacent organs, how many lymph nodes it has metastasized to (if any), and whether it has spread to distant organs. According to the most commonly used staging system, American Joint Committee on Cancer (AJCC) TNM (Tumor, Node, Metastasis), colorectal cancer can be classified into five general groups: stages 0, I, II, III, and IV, where stage 0 refers to the earliest stage disease, cancer *in situ* (i.e. abnormal cells that have not invaded other tissue, sometimes called pre-cancerous), and stage IV refers to the most advanced disease, cancer that has spread from the primary site to distant organs.

Surgery is usually the main treatment for early stage CRC, however, for late stage CRC or for individuals that have higher risk for recurrence, additional treatment, such as chemotherapy or radiotherapy, may be needed in order to improve prognosis. Both chemotherapy and radiotherapy attempt to kill or impede the growth of cancer cells that were not removed by surgery. Chemotherapy is often given after surgery to kill tumor cells that may not have been removed by surgery or which may have metastasized to other parts of the body; radiotherapy is given either before surgery for the purpose of shrinking the tumor to facilitate its removal, or

after surgery to help prevent cancer from recurring in the area from which the tumor was removed.

Postoperative chemotherapy, known as adjuvant chemotherapy, has been a component of the standard treatment for stage III colon and stage II/III rectal cancer since the early 1990s. In the 1990 US National Institute of Health (NIH) Consensus Conference, 5-fluorouracil (5-FU)-based adjuvant chemotherapy was recommended as the standard treatment for stage III colon cancer; 5-FU-based adjuvant chemotherapy combined with radiotherapy was recommended as the standard treatment for stage II/III rectal cancer. This recommendation was based on multiple randomized trials which demonstrated that the addition of 5-FU-based chemotherapy over surgery alone caused a relative risk reduction of 41% for recurrence and 33% for mortality in patients with stage III colon adenocarcinoma,<sup>6-8</sup> and the addition of adjuvant chemotherapy plus radiotherapy for stage II/III rectal cancer caused a relative risk reduction of 36% for recurrence and of 29% for mortality.<sup>9-11</sup>

Over the past years, many advances have been achieved in understanding and treating CRC.<sup>12</sup> For example, advanced techniques including laparoscopic- and robotic-assisted surgery has been used in treating colon cancer. Total mesorectal excision (TME) has become a new standard of surgery for rectal cancer.<sup>13</sup> More chemotherapy drug options, such as oxaliplatin<sup>14</sup> and capecitabine,<sup>15</sup> were introduced in clinical practice. Specific treatment recommendations have been continuously updated and integrated based on new evidence.<sup>16-18</sup> The standard treatment modality for stage III colon cancer, i.e. surgery followed by adjuvant chemotherapy, however, has not changed. For rectal cancer, preoperative radiotherapy has been an acceptable alternative

to postoperative radiotherapy<sup>17</sup> and in recent years preoperative chemoradiotherapy has become popular,<sup>19</sup> however, adjuvant chemotherapy remains an important component of standard treatment for stage II/III rectal cancer.<sup>18</sup>

Despite guideline recommendations, numerous studies have demonstrated underuse of adjuvant chemotherapy among patients with stage III colon or stage II/III rectal cancer.<sup>20-26</sup> In two recent population-based studies conducted in Alberta, Canada, where standard cancer care for all permanent residents is covered through provincial healthcare insurance, approximately 50% of patients diagnosed in 2002-2005 with stage III colon<sup>1</sup> and 46% of patients with stages II/III rectal adenocarcinoma<sup>2</sup> did not receive guideline-based adjuvant chemotherapy. Such a finding is surprising given that the treatment guideline has been in place for 12-15 years and standard cancer care is free to patients.

In Alberta, all non-surgical cancer treatment is provided through cancer care facilities that are coordinated and operated provincially by Alberta Health Services, Cancer Care. Typically, for asymptomatic disease, diagnosis of CRC may start with a CRC screening test, known as fecal occult blood test (FOBT) or fecal immunochemical test (FIT). For symptomatic disease, the diagnosis starts with a visit to family physician, from whom the patient may get a referral for lab tests or a referral to a specialist (a surgeon or gastroenterologist in order to have a colonoscopy conducted). Diagnosis of CRC is made through a series of tests. Colonoscopy is the gold standard for diagnosis of CRC. Flexible sigmoidoscopy, or barium enema can also be used as alternatives to colonoscopy for patients with major comorbidities. A digital rectal examination, endoscopic ultrasound, and/or magnetic resonance imaging (MRI) provide additional

information about the extent of the disease (e.g. depth of penetration, lymph node involvement, fixation to adjacent structures). A computed tomography (CT) scan of the thorax, abdomen, and pelvis is also recommended to exclude the possibility of metastatic disease and to provide a baseline for the future surveillance CT scans. A pre-operative carcinoembryonic antigen (CEA) assay is recommended for future comparison. A positron emission tomography (PET) is recommended if the conventional diagnostic work-up fails to localize disease in the context of an asymptotically elevated post-operative CEA.<sup>27, 28</sup>

After the cancer is diagnosed and staged, treatment is planned and carried out. Neoadjuvant treatment with chemotherapy and/or radiation may be carried out before surgery in cases in which the cancer is locally-advanced. For cancer amenable to surgical resection, a surgery will be scheduled and performed in a hospital by a general surgeon or a surgical oncologist. The definitive stage of cancer is determined by pathologic analysis of the tumor specimen removed at surgery. After surgery, the surgeon is responsible to refer the patient to an oncologist to discuss the need for further treatment. Chemotherapy or radiotherapy can only be prescribed by an oncologist or a general physician with specific training in oncology who works in cancer care facilities. There are 17 cancer care facilities throughout the province, six of which have oncologists on site to provide consultations with patients (including two tertiary cancer centers located in the two metropolitan areas Edmonton and Calgary, and four associate cancer centers in four smaller cities). To receive chemotherapy or radiotherapy, a patient must get a referral and attend an oncologist consult, and have treatment recommended by the oncologist.

In a provincially-funded healthcare system, patients should have equitable access to standard care regardless of care providers. Previous studies, however, have demonstrated that not having an oncologist-consult was one of the main barriers to receiving adjuvant chemotherapy and the rate of oncologist-consult varied considerably across surgical hospitals that refer patients to oncologists, after adjusting for case-mix.<sup>1, 2, 29</sup> It is unknown whether the pattern of adjuvant treatment differs by oncologist for those patients who had an oncologist-consult. To better understand the sources of variation in receipt of adjuvant chemotherapy, a study was conducted to examine the variation across oncologists in the probability of patients who received adjuvant chemotherapy. The detail of this study is reported in Chapter 2.

Cancer is the leading cause of deaths in Canada. According to the most recent statistics, about 75,000 deaths (29% of all deaths) were caused by cancer in 2011.<sup>5</sup> With population growth and aging, the number of deaths from cancer is expected to increase in future. The need for efficient EOL care services for cancer patients will, therefore increase.

Quality of EOL care is gaining attention as a key measure of excellence in cancer care. Calls for research on EOL care have increased over time.<sup>30-32</sup> In the mid-2000s, researchers at U.S. Dana-Farber Cancer Institute developed a set of population-based quality indicators for evaluating EOL care services for cancer patients.<sup>33</sup> Some indicators were considered as measures for intensiveness of use of EOL care, including continuation of chemotherapy near death, frequent

emergency room (ER) visits, hospital admissions, admission to intensive care units (ICU) at the end of life, death in an acute care setting, and lack of palliative or hospice care. The rationale for using these indicators to assess the quality of EOL care for terminally ill cancer patients is: 1) continuation of anti-cancer treatment such as chemotherapy very near death may indicate overuse of treatment; 2) high rates of acute care use, such as frequent emergency room (ER) visits, hospitalizations, and intensive care units (ICU) admission near the end of life, may indicate lack of coordinated care focused on palliation and support; 3) an ideal death setting should be one with palliative and supportive care, neither of which are typically available in an acute care hospital environment. A high proportion of deaths in acute care hospitals, therefore, may indicate lack of hospice or palliative care.<sup>33</sup>

Some of these quality indicators have been tested and validated in Ontario and Nova Scotia, Canada.<sup>34</sup> Although not all indicators have been accepted and considered meaningful by all relevant stakeholders (e.g. patients, family, care givers and health professionals), some indicators have been recommended as useful tools for monitoring a cancer care system.<sup>35, 36</sup> Related information and research, however, is lacking in Alberta. The second study described herein, measured the quality of EOL cancer care using the following five quality indicators: use of chemotherapy, ER visit, hospitalization, ICU admission, and death in acute-care hospital. This study is reported in Chapter 3.

### **1.3 Objectives**

- 1) To assess the relationship between oncologist and receipt of guideline-recommended adjuvant chemotherapy, i.e. to test the null hypothesis that rates of receiving adjuvant chemotherapy for patients with resected stage III colon or stage II/III rectal adenocarcinoma are equal across oncologists in Alberta; and to quantify the oncologist-specific probability/odds of patient's not receiving adjuvant chemotherapy.
  
- 2) To measure the indicators related to aggressive use of healthcare near the end of life among patients who died of CRC in Alberta in 2006-2009 and to identify potential factors that are related with aggressive EOL care utilization.

### **1.4 Significance**

Study 1 is the first study to assess variation in oncologists' treatment patterns with respect to adjuvant chemotherapy for colorectal cancer. Study 2 is the first attempt in Alberta to measure the quality of EOL cancer care using validated quality indicators. These two population-level studies, respectively, address important aspects of CRC care during two distinct and important points of care, treatment and EOL. Findings from this work could provide important information for healthcare professionals and policy makers in identifying and implementing interventions that address barriers to optimal care as well as motivate further research.

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## Chapter 2 Variation by Oncologist in Treatment Patterns of Adjuvant Chemotherapy for Colorectal Cancer

### 2.1 Introduction

5-FU-based adjuvant chemotherapy has been the standard treatment for surgically-resected patients with stage III colon or stage II/III rectal adenocarcinoma since the National Institute of Health (NIH) Consensus Conference in 1990.<sup>1</sup> Multiple randomized controlled clinical trials and pooled analyses have demonstrated that adjuvant chemotherapy significantly reduces the frequency of recurrence and improves survival for patients with stage III colon cancer<sup>2-8</sup> and stage II/III rectal cancer,<sup>9-12</sup> compared with patients treated with surgery alone. Several population-based studies in North America have found, however, that a significant proportion of colorectal cancer patients who are potentially eligible for adjuvant chemotherapy do not receive it.<sup>13-22</sup> A series of studies conducted in Alberta, Canada, found that approximately 50% of surgically treated stage III colon and stage II/III rectal cancer patients diagnosed in 2002-2005 did not receive adjuvant chemotherapy<sup>23,24</sup> and poorer survival for untreated patients was observed compared with patients who received timely adjuvant chemotherapy.<sup>25</sup>

Given the proven efficacy and safety of adjuvant chemotherapy, it is important to identify barriers related to low utilization and develop targeted interventions to improve it. Risk factors associated with not receiving adjuvant chemotherapy identified to date have mainly focused on patient characteristics.<sup>13-16, 18, 22-24</sup> There are, however, other important factors in the health care system that likely affect utilization of adjuvant chemotherapy such as practice patterns of treating

physicians. The objective of this study was to investigate the effect of the consulting oncologist on non-receipt of adjuvant chemotherapy and to assess the extent of variation in prescribing adjuvant chemotherapy by oncologists in Alberta.

In Alberta, all non-surgical cancer treatments are administered in provincially-coordinated and accredited cancer care facilities. In order to receive adjuvant chemotherapy, a patient must be referred to and consult an oncologist, the oncologist must recommend it, and the patient must accept it. There are six cancer facilities located throughout the province in which an oncologist-consult may be conducted. Under this mechanism, there are three possibilities leading to a patient not receiving adjuvant chemotherapy: 1) the patient did not have an oncologist-consult; 2) the patient had an oncologist-consult but the oncologist did not recommend chemotherapy; or 3) the patient declined adjuvant chemotherapy. Previous studies found that 20% of all surgically-treated stage III colon or stage II/III rectal cancer patients did not have an oncologist-consult<sup>23</sup> and that the hospital in which their surgery occurred was associated with whether they had an oncologist-consult indicating important variation in referral patterns.<sup>26</sup> In the current study we extend the examination of variation in treatment patterns to the oncologist. Specifically, we assessed whether there is a relationship between the consulting oncologist and patient non-receipt of adjuvant chemotherapy.

## 2.2 Methods

### 2.2.1 Study Population

All surgically-treated patients diagnosed with stage III colon (ICD-O 3<sup>rd</sup> edition<sup>27</sup> site code c18.0, C18.2-18.9), stage II rectal (ICD-O<sup>27</sup> site code c20.9) or stage III rectal cancer (ICD-O<sup>27</sup> c19.9 or c20.9) in years 2002 to 2005 in Alberta, Canada, were identified from the Alberta Cancer Registry. Cancer stage was determined using the American Joint Committee on Cancer (AJCC) *AJCC Cancer Staging Manual, 6<sup>th</sup> edition*.<sup>28</sup> Stage II was defined as an invasive tumor (T3: more than 5 cm in size or T4: any size that invaded adjacent organs) that has not spread to regional lymph nodes (N0) nor distant metastatic sites (M0). Stage III was defined as a tumor of any size (T1-4) that has spread to one or more regional lymph nodes (N1-3) but not to distant metastatic sites (M0).<sup>28</sup> The Alberta Cancer Registry has been in existence since 1942 and is regularly awarded the highest degree of certification for data completeness by the North American Association of Comprehensive Cancer Registry.<sup>29</sup>

Patients were excluded if they: 1) had a tumor histology other than adenocarcinoma; 2) died within 7 days of diagnosis; 3) had another cancer diagnosed within 6 months prior or subsequent to their colorectal cancer diagnosis; 4) were treated outside of Alberta; or 5) did not have an oncologist-consult within four months after surgery to discuss treatment options. Quality assurance activities found that oncologist-consults more than four months post-surgery were for disease progression, not initial treatment planning.

### 2.2.2 Data Sources

Additional information obtained from the cancer registry included patient demographics, initial treatment modalities and their start dates. In the case of missing or incomplete dates of adjuvant chemotherapy, the cancer electronic medical record (EMR) was reviewed to retrieve the information and/or to confirm whether treatment was received in Alberta. Data from the cancer EMR have been used extensively for operational and research purposes since 2002 and have been proven to be accurate and complete for the purposes used. The date of the oncologist-consult, the consulting oncologist, and the cancer facility were also obtained from the cancer EMR. The consulting oncologist for each patient was defined as the oncologist seen at the first post-operative oncologist-consult within four months post-surgery. If a patient did not have an oncologist-consult within four months after surgery but had a pre-operative consult to discuss treatment options, then the oncologist seen at the pre-operative consultation was assigned as the patient's consulting oncologist.

Patient co-morbidities were obtained from two provincial hospital databases: 1) the Ambulatory Care Classification System that contains outpatient data from all Alberta hospitals; and 2) the Discharge Abstract Database that contains inpatient data from all Alberta hospitals. Diagnosis codes in these two databases that occurred within one year prior to the colorectal cancer diagnosis were used to calculate co-morbidity scores. Modified Charlson co-morbidity scores were calculated as described by Deyo *et al.*<sup>30</sup> using updated algorithms developed by Quan *et al.*<sup>31</sup> Depending on the year, the International Classification of Diseases version 9-Clinical Modification (ICD-9-CM) or ICD-10-Canada (ICD-10-CA) codes were used.

Ethical approval for this study was obtained from the Alberta Cancer Research Ethics Committee.

### 2.2.3 Statistical Analysis

Proportions of patients who did not receive adjuvant chemotherapy with respect to patient clinical/demographic characteristics were calculated stratified by tumor site and stage. Chi-square or Fisher's exact tests, as appropriate, were used to assess associations between categorical variables and not receiving adjuvant chemotherapy. The Cochran-Armitage trend test was used to evaluate the association for age and co-morbidity. All tests are two-sided. SAS software (version 9.2; SAS Institute, Cary, NC) was used for these analyses.

In the case-mix adjusted analysis, a generalized linear mixed model<sup>32</sup> was used to estimate the oncologist-specific odds ratio for patients' not receiving adjuvant chemotherapy. The *xtmelogit* command in Stata software was used (version 11.1; Stata Cooperation, College Station, TX).

Specifically, the model took the following form:

$$\text{logit} \{P(Y_{ij} | \mathbf{b}_{1i}, \mathbf{b}_{2i}, \mathbf{b}_{3i})\} = \beta_0 + \beta_1 \text{sex} + \beta_2 \text{age1} + \beta_3 \text{age2} + \beta_4 \text{age3} + \beta_5 \text{comorbidity1} + \beta_6 \text{comorbidity2}^+ + \mathbf{b}_{1i} \mathbf{R2}_{ij} + \mathbf{b}_{2i} \mathbf{R3}_{ij} + \mathbf{b}_{3i} \mathbf{C3}_{ij},$$

where  $Y_{ij}$  is an indicator for not receiving adjuvant treatment for the  $j^{\text{th}}$  patient of the  $i^{\text{th}}$  oncologist, and  $b_{1i}, b_{2i}, b_{3i}$  are the oncologist-specific log odds ratios of not receiving adjuvant chemotherapy, relative to the overall average, for their patients with stage II rectal, stage III rectal, and stage III colon cancer, respectively. The  $Y_{ij}$ 's were assumed to follow independent Bernoulli distributions with probabilities  $\Pr(Y_{ij} | \mathbf{b}_{1i}, \mathbf{b}_{2i}, \mathbf{b}_{3i})$ 's, conditioned on the oncologist-specific random-effect vector  $(\mathbf{b}_{1i}, \mathbf{b}_{2i}, \mathbf{b}_{3i})$  which was assumed to follow a multivariate normal

distribution with means zero and an unstructured variance-covariance matrix  $\Sigma$ . Sex, age at diagnosis (entered as a natural cubic spline with 4 knots), and co-morbidity score were included in the model as fixed-effect covariates. Empirical Bayes estimation<sup>33</sup> was used to estimate the adjusted oncologist-specific log odds ratios and their 95% confidence intervals.

Scatter plots and simple linear regression were used to examine the relationship between patient volume and estimated adjusted oncologist-specific odds ratio of patients not receiving adjuvant chemotherapy.

### **2.3 Results**

There were 1,652 patients with surgically resected stage III colon or stage II/III rectal cancer diagnosed in years 2002-2005 in Alberta. We excluded 373 patients for one or more of the following reasons: 276 did not have an oncologist-consult within four months post-surgery; 16 patients had a tumor histology other than adenocarcinoma; 16 died within seven days of diagnosis; 67 had another cancer diagnosed within six months prior or subsequent to their colorectal cancer diagnosis; and 2 were treated outside of Alberta. The remaining 1,279 patients were included: 252 patients had stage II rectal cancer, 414 had stage III rectal cancer and 613 had stage III colon cancer. The consulting oncologists were identified from the post-surgical consultation for 1,234 patients and from the pre-surgical consultation for 45 patients.

Colorectal cancer related consultation was conducted by 45 oncologists, 23 of whom conducted 95% of the consultations. Thirty-five oncologists consulted stage II rectal cancer patients (range

of patient volume: 1-36), 37 consulted stage III rectal cancer patients (range of patient volume: 1-58), and 35 consulted stage III colon cancer patients (range of patient volume: 1-124).

In total, 371 (29.0%) patients did not receive adjuvant chemotherapy after an oncologist-consult. Table 2.1 shows the relationship between not receiving adjuvant chemotherapy and patient demographic/clinical characteristics. Patients with stage II rectal cancer were the least likely and those with stage III rectal cancer were the most likely to receive adjuvant chemotherapy. In each tumor stage/type stratum, the percentage of patients who did not receive adjuvant chemotherapy increased significantly with age and co-morbidity score but did not significantly vary by sex, year of diagnosis, or cancer facility.

Similarly, in the case-mix adjusted analysis, co-morbidity score was strongly associated with non-receipt of adjuvant chemotherapy. Compared to patients without any co-morbidities, the adjusted odds ratio of not receiving adjuvant chemotherapy for patients with a co-morbidity score of 1 was 1.99 (95% CI: 1.27, 3.12); and for patients with a score of 2 or more it was 2.96 (95% CI: 2.20, 3.99). Age was also a significant factor in the case-mix adjusted model ( $P < .0001$ ). Sex was not associated with non-receipt of chemotherapy ( $P = .37$ ). There were no significant two-way interactions between age, sex, and co-morbidity.

After adjusting for the case mix, there was strong evidence against homogeneity among oncologists in terms of patients' not receiving adjuvant chemotherapy ( $P < .0001$ ). Moreover, the oncologist-specific random effects between each pair of tumor site/stage strata were highly

positively correlated: 0.96 between stage II and III rectal cancers; 0.90 between stage III colon and stage III rectal cancers; and 0.74 between stage III colon and stage II rectal cancers.

Figure 2.1 displays the estimated oncologist-specific case-mix adjusted odds ratios for patients' not receiving adjuvant chemotherapy, compared to the overall Alberta average. For the 35 oncologists that consulted patients with stage II rectal cancer, the oncologist-specific case-mix adjusted odds ratios for not receiving adjuvant chemotherapy varied from 0.26 to 16.75. For the 37 oncologists that consulted patients with stage III rectal cancer, the oncologist-specific case-mix adjusted odds ratios varied from 0.43 to 4.50. For the 35 oncologists who consulted patients with stage III colon cancer, the oncologist-specific case-mix adjusted odds ratios ranged from 0.55 to 1.95.

Of the 23 oncologists who saw 95% of the patients, 10 of them were significantly or marginally (confidence interval includes 1.0 but does not go beyond 0.86) less likely to give their patients adjuvant chemotherapy than the provincial average in at least two of the tumor stage/type strata; patients of four oncologists were less likely to receive adjuvant chemotherapy in all three strata.

No significant linear relationship was found between the estimated oncologist-specific log odds ratios of patients' not receiving adjuvant chemotherapy and the patient volume in any of the three tumor stage/site strata (Figure 2.2). The estimated slope from simple linear regression was 0.03 ( $P = .097$ ) for stage II rectal cancer; 0.01 ( $P = .085$ ) for stage III rectal cancer; and -0.0003 ( $P = .89$ ) for stage III colon cancer.

## 2.4 Discussion

Overall, 29% of potentially eligible patients with surgically resected stage III colon or stage II/III rectal cancer diagnosed in 2002-2005 did not receive adjuvant chemotherapy after their oncologist-consult. There are three main findings related to the variation in practice patterns found: 1) the magnitude of variation among oncologists varies by tumor site and stage, which is largest for stage II rectal cancer and smallest for stage III colon cancer; 2) within oncologists, there is relative consistency in propensity to use or not use adjuvant chemotherapy across the three tumor strata; 3) approximately half of the oncologists who saw the majority of the patients (10 of 23 oncologists) were significantly or marginally less likely to give adjuvant chemotherapy to their patients than the provincial average in two or three of the tumor stage/type strata.

The observed variation amongst oncologists likely reflects differing opinions by individual oncologist towards adjuvant chemotherapy in spite of the fact that adjuvant chemotherapy has been shown to provide a significant survival advantage to patients with stage III colon and stage II/III rectal cancer over surgery alone.

The relatively small variation in oncologist-specific adjusted odds ratio of non-receipt of chemotherapy for stage III colon cancer (Figure 2.1) suggests a higher level of consensus in use of adjuvant chemotherapy among oncologists for stage III colon cancer. In contrast, the wider variation among oncologists for rectal cancer, especially for stage II rectal cancer, suggests lower consensus among oncologists in treatment of rectal cancer and the influence of the individual oncologist in determining the use of adjuvant therapy for stage II/III rectal cancer patients. The disparity between colon and rectal cancer treatment may reflect different management strategies

for each, despite the similarity in treatment guidelines for both. Treatment guidelines for stage II/III rectal cancer are more complex than those for stage III colon cancer because of the role and timing of radiation therapy. Related to this is a debate regarding the relative advantages of pre-operative radiotherapy/chemoradiotherapy vs. post-operative chemoradiotherapy and pre-operative radiotherapy/chemoradiotherapy only vs. plus adjuvant chemotherapy.<sup>34-38</sup> At the time of this study, however, neo-adjuvant radiation or chemoradiation was relatively new and, therefore, uncommon. To date, however, adjuvant chemotherapy remains part of the standard treatment guidelines for stage II/III rectal cancer patients in Canada.<sup>39</sup>

Because both referring and treating physicians play important roles for patients to receive guideline-adherent treatment, the variation in treatment patterns observed among oncologists in this study is worth comparing to the previous study that examined the variation in referral patterns among surgeons to oncologists.<sup>26</sup> The primary similarities of the previous findings to this study were that patients with stage II rectal cancer were least likely, and those with stage III rectal cancer were most likely, to be referred to an oncologist for consultation and that patient volume was not associated with the referral rate. In contrast to the current study, however, the probability to refer or not refer patients to an oncologist varied by tumor type/stage stratum within hospitals; that is, unlike the oncologists with respect to treatment, there was not a general propensity to refer or not to refer within a hospital. Findings from these two studies suggest that surgeons and oncologists have different behaviors regarding treatment of patients with stage III colon or stage II/III rectal cancer, although there is a general propensity amongst both groups to facilitate post-surgical treatment less frequently for patients with stage II rectal cancer than for those with stage III rectal or colon cancer.

There have been two national surveys conducted in the United States, to assess physicians' attitudes and beliefs (both surgeons and oncologists) in treating stage III colon cancer patients with adjuvant chemotherapy.<sup>40, 41</sup> One of these studies found differing preferences amongst surgeons and oncologists regarding treating patients with chemotherapy based on patient age, and types and severities of comorbidities.<sup>41</sup> Although the survey did not include scenarios for stage II/III rectal cancer patients, this finding is consistent with ours in that surgeons and oncologists behaved differently with respect to supporting adjuvant chemotherapy for their patients. Also consistent with the current study was that neither survey found a relationship between patient volume and propensity to prescribe adjuvant chemotherapy.

Strengths of this study are that it includes the entire population of relevant patients in a Canadian province over a four-year period. To our knowledge, it is the first study that profiles the variability by individual oncologists in treatment utilization for colorectal cancer patients. Applying the random-effect model and empirical Bayes estimates to profile the oncologist performance has methodological advantages that allowed us to calculate the oncologist-specific odds ratio/probability which can be interpreted in a clinically meaningful but straightforward way. Corresponding data sources as used in this study are available in other Canadian provinces so the study methods are replicable in other Canadian jurisdictions and likely, elsewhere.

The major limitation to the study is that it used data that are electronically readily available. Not all variables that affect treatment decisions are available from such data sources such as post-surgical functional status, contraindications to chemotherapy (e.g., allergy) and patient refusal. It is unlikely, however, that a given oncologist would have a higher percentage of patients with these and similar issues than other oncologists; therefore, it is unlikely that these factors would explain the differences in treatment patterns by oncologist that we found. It is possible, however, that adjustment for a broader set of variables would decrease the variation across oncologists. Finally, treatment planning may be multidisciplinary; treatment decisions at the time of consultation may be affected by care providers in addition to oncologists.

To better understand the causes of variation in clinical practice and to develop strategies to increase the use of adjuvant treatment for colorectal cancer patients, future studies need to identify ways to improve patient-provider interaction/communication and identify influences on both patient and physician decision making. To enhance adherence to standard treatment, a coherent referral relationship between surgeons and oncologists is important as is good physician-patient communication and trust.

## **2.5 Conclusion**

In summary, this work demonstrates important variation by oncologist in their treatment patterns relative to standard treatment guidelines for stage II/III colorectal cancer. In order to increase consistency with treatment guidelines and decrease variation in treatment patterns, we are embarking on knowledge translation activities related to heightening awareness of current

practice variation, the impact on patient outcomes, and discussion on the level of variation that would be deemed reasonable for surgeons and oncologists.

## **2.6 Acknowledgement**

The authors would like to thank Charlotte King, John Fleming and Xue Li from Alberta Health Services for assistance in obtaining and preparing the data for analysis and Angela Bella for assistance in formatting figures and references of this manuscript.

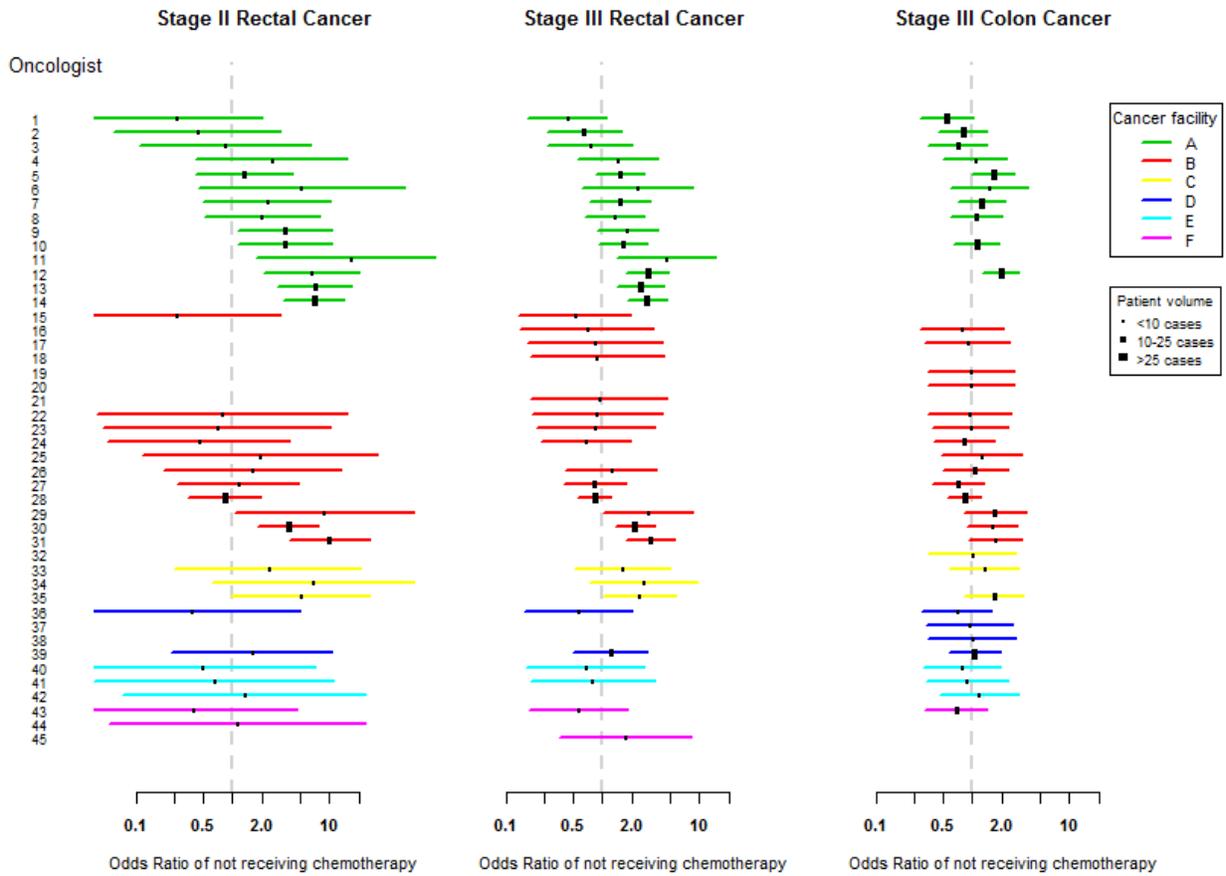
**Table 2.1 Association between patient characteristics and not receiving adjuvant chemotherapy by cancer stage/type**

Characteristics	Stage II rectal cancer		Stage III rectal cancer		Stage III colon cancer	
	Had a consult	No adjuvant chemotherapy	Had a consult	No adjuvant chemotherapy	Had a consult	No adjuvant chemotherapy
	<i>N</i>	<i>n</i> (%)	<i>N</i>	<i>n</i> (%)	<i>N</i>	<i>n</i> (%)
<b>Total</b>	252	103 (40.9)	414	106 (25.6)	613	162 (26.4)
<b>Sex</b>		<i>P</i> = .67		<i>P</i> = .87		<i>P</i> = .91
Female	77	33 (42.9)	163	41 (25.2)	286	75 (26.2)
Male	175	70 (40.0)	251	65 (25.9)	327	87 (26.6)
<b>Age at diagnosis<sup>b</sup></b>		<i>P</i> < .0001		<i>P</i> < .0001		<i>P</i> < .0001
Mean[SD]	65.1[11.4]	70.0[11.3]	63.4[12.0]	71.7[11.0]	66.2[12.0]	75.4[9.2]
Median	65.0	72.0	65.0	73.0	68.0	78.0
<65	123	30 (24.4)	204	18 (8.8)	257	19 (7.4)
65-75	79	34 (43.0)	147	44 (29.9)	190	44 (23.2)
>75	50	39 (78.0)	63	44 (69.8)	166	99 (59.6)
<b>Charlson Comorbidity Index<sup>b</sup></b>		<i>P</i> = .0007		<i>P</i> < .0001		<i>P</i> < .0001
0	223	83 (37.2)	363	81 (22.3)	456	89 (19.5)
1	19	12 (63.2)	37	15 (40.5)	97	33 (34.0)
≥2	10	8 (80.0)	14	10 (71.4)	60	40 (66.7)
<b>Year of diagnosis</b>		<i>P</i> = .21		<i>P</i> = .54		<i>P</i> = .64
2002	56	17 (30.4)	84	22 (26.2)	144	33 (22.9)
2003	57	25 (43.9)	94	22 (23.4)	168	43 (25.6)
2004	61	30 (49.2)	112	34 (30.4)	142	40 (28.2)
2005	78	31 (39.7)	124	28 (22.6)	159	46 (28.9)
<b>Cancer facility<sup>c</sup></b>		<i>P</i> = .49		<i>P</i> = .30		<i>P</i> = .64
A	121	56 (46.3)	206	61 (29.6)	308	86 (27.9)
B	109	39 (35.8)	158	34 (21.5)	198	51 (25.8)
C	8	4 (50.0)	13	4 (30.8)	23	7 (30.4)
D	5	1 (20.0)	20	5 (25.0)	41	8 (19.5)
E	7	2 (28.6)	8	0 (0)	18	6 (33.3)
F	2	1 (50.0)	9	2 (22.2)	25	4 (16.0)

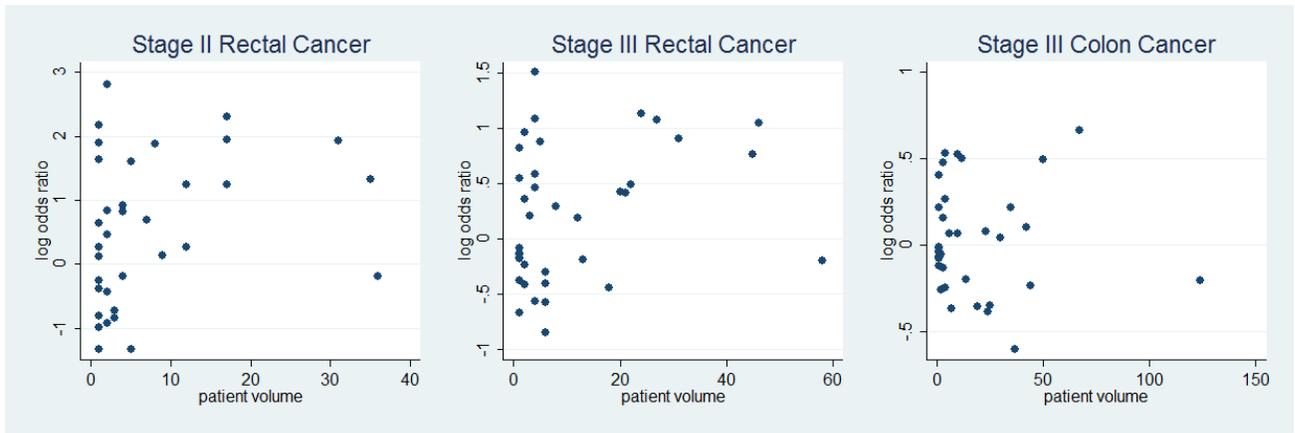
<sup>a</sup> Percentages are row percentages with the number who had consult as the denominator.

<sup>b</sup> P-values for age and co-morbidity were calculated by the Cochran-Armitage Trend Test.

<sup>c</sup> P-values were calculated by Fisher's exact test.



**Figure 2.1** Forest plots of the oncologist-specific case-mix adjusted odds ratios and 95% confidence intervals for patients not receiving adjuvant chemotherapy. Each line on the same row represents odds ratio estimates for one oncologist. If the oncologist did not have any patients with a particular tumor type/stage, there is a blank in the corresponding oncologist-specific space.



**Figure 2.2** Scatter plots for the estimated oncologist-specific log odds ratio for patients not receiving adjuvant chemotherapy vs. patient volume.

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## **Chapter 3 Aggressiveness of End-of-life Care for Colorectal Cancer Patients in Alberta, Canada: 2006-2009**

### **3.1 Introduction**

Quality of end-of-life (EOL) care is gaining increasing attention as a key facet of excellence in cancer care.<sup>1</sup> In Canada, cancer is the leading cause of death and accounts for approximately 30% of all deaths annually.<sup>2</sup> Despite advances in cancer survival, deaths from cancer among Canadians will increase over the next decade due to a combination of population growth and aging.<sup>3</sup> Studies in the United States and Canada have documented important practice variation and deficiencies in EOL cancer care, such as inadequate management of pain and symptoms, trends towards treating dying patients more aggressively, and disparities in access to palliative care or hospice services.<sup>4-13</sup> Identifying gaps in the quality of EOL care in order to improve it is, therefore, important.

Measuring the quality of EOL care is essential to knowing where healthcare system can improve its EOL care.<sup>14</sup> A population-based description of healthcare services used at the EOL can provide valuable information and insight to decision makers for identifying priority areas for appropriate intervention.<sup>15</sup> A set of quality indicators for EOL cancer care have been proposed and validated in United States.<sup>16, 17</sup> These indicators are a combination of measures of overly aggressive care and underuse of supportive care services such as hospice or palliative care. They have been tested in two provinces of Canada and are considered to be relevant and useful tools for quality assessment and monitoring of EOL cancer care.<sup>18, 19</sup> The purpose of the current study

is to evaluate aggressiveness of EOL care in Alberta, Canada, by using individuals who died of colorectal cancer (CRC) in 2006-2009 in the province.

## **3.2 Methods**

### *3.2.1 Study Design and Cohort Selection*

A population-wide retrospective study was conducted that included all patients who died of invasive CRC in Alberta, Canada between Jan 1, 2006 and Dec 31, 2009. Cases were identified through the Alberta Cancer Registry, a population-based cancer registry that covers the province's population of 3.6 million and receives provincial vital statistics monthly and national updates annually. Cases were excluded if age at death was less than 20 years, if they died within 30 days after CRC diagnosis, or if they were diagnosed with another stage IV cancer after their CRC diagnosis.

### *3.2.2 Data Sources and Variables*

Demographics and clinical characteristics including sex, age at death, region of residence, date and cause of death, site and stage of tumor at diagnosis, duration of CRC, history of other cancers, were obtained from the Alberta Cancer Registry. The Alberta Cancer Registry was established 1942 and is regularly awarded the highest degree of certification for data completeness, accuracy and timeliness by the North American Association of Comprehensive Cancer Registries.<sup>20</sup> Region of residence was categorized into five geographic areas, corresponding to healthcare zones. Two zones are urban and suburban in population size and density (Edmonton and Calgary) and three zones are mixture of suburban, rural and remote

regions (South, Central and North). Tumor site was classified as colon (C18), rectosigmoid (C19) or rectum (C20), based on the International Classification of Diseases for Oncology version 3 (ICD-O-3).<sup>21</sup> Cancer stage was classified using American Joint Committee on Cancer (AJCC) Cancer Staging Manual 6<sup>th</sup> edition.<sup>22</sup> Duration of disease was the time interval between the diagnosis date of the CRC with the highest stage at diagnosis and the date of death.

Two provincial administrative healthcare databases were used to identify hospital-related events and the Charlson co-morbidity index: the Ambulatory Care Classification System which includes data on all outpatient visits to all hospitals in the province; and the Discharge Abstract Database which includes diagnostic and procedure codes for all inpatient hospital admissions in the province. The former was used to identify emergency room (ER) visits and the latter was used to identify all hospital admissions, intensive care unit (ICU) admissions, and in-hospital deaths. Additionally, diagnosis codes (as per ICD-10-CM) in the last year of life from these two databases, were used to calculate the Charlson co-morbidity index for each patient based on the updated algorithms developed by Quan *et al.*<sup>23</sup> and modified by Deyo *et al.*,<sup>24</sup> excluding codes for primary or metastatic cancer.

In Alberta, standard cancer care is free to residents through the provincial health care insurance system. Oncology services except surgery are administered and delivered in provincially coordinated cancer care facilities. There are 17 cancer care facilities throughout the province, six of which have oncologists on site to provide treatment consultations to patients. The 11 community cancer centers provide chemotherapy, education and support for cancer patients upon referral. The electronic cancer medical record captures information on all visits and services

received in cancer facilities. Dates of each of the following care services were obtained from this database: initial consultation and follow-up visits with an oncologist, chemotherapy and radiotherapy. This database has been used extensively for operational and research purposes and shown to be of high quality.<sup>25-27</sup>

For each case, a unique anonymized identifier was created for data linkage and analysis. Quality assurance and cross checks were performed on datasets during and after data linkage to ensure accuracy and completeness.

### 3.2.3 Outcome Variables

Five quality indicators as defined and validated by Earle *et al.*<sup>16</sup> were adopted as the primary outcomes. They included: receiving chemotherapy in the last 14 days of life; having more than one ER visit, more than one hospitalization, and any ICU admission, in the 30 days of life; and dying in an acute care hospital.

### 3.2.4 Statistical Analysis

For each of the five indicators of aggressive EOL care, the proportion of patients who received the type of aggressive care specified by the indicator was calculated. In the unadjusted analysis, Chi-square tests were used to assess the association between potential explanatory variables and each indicator; Cochran-Armitage trend tests were used for assessing the trend in the association for age, time from diagnosis to death and co-morbidity index. Multivariable logistic regression was conducted to examine adjusted associations of explanatory variables with each indicator of

aggressive EOL care. Potential explanatory variables were sex, age, region of residence, year of death; cancer site, cancer stage, comorbidity, history of other cancer; having oncology consult, having oncologist follow-up care, receiving radiotherapy, and receiving chemotherapy, in the last 6 months of life. All of the potential explanatory variables were included in the model without variable selection. Interaction between tumor stage and duration was assessed for each logistic model. Continuous variables were examined both as continuous and categorical in exploratory analyses but fitted categorically in the regression analyses, where cutoff points for categorizing continuous variables were based on data distribution and/or clinical indication. Because all the five indicators potentially represent the aggressiveness of EOL care, a composite measure of the five indicators were generated and categorized into three groups: had 0 indicator; had 1 indicator; and had 2 or more indicators. Polytomous logistic regression was performed to determine risk factors for having one or more indicators of aggressive EOL care.

Additionally, in order to assess the outcome variables over a longer period of time, chemotherapy use in the last 6 months and last 30 days of life, had multiple ER visits, multiple hospitalizations and one ICU admission in the last 6 months, were examined using the same methods as described above for the primary outcome measures. Results are shown in Appendices 3.1-3.3.

Based on the ambulatory or inpatient data, we calculated the most common diagnoses for multiple ER visits, multiple hospitalizations and ICU admission in the last 30 days of life (Appendices 3.4-3.6). The most common diagnoses were collapsed based on ICD-10 category. All statistical analyses were performed using SAS 9.2 (SAS Institute, Cary, NC).

### 3.3 Results

A total of 2,296 patients were identified with CRC as the documented cause of death in Alberta between 2006 and 2009. Two hundred and twenty-two patients were excluded for one of the following reasons: the age at death was less than 20 years old ( $n = 1$ ), died within 30 days of diagnosis ( $n = 212$ ), or diagnosed with another stage IV cancer after their CRC diagnosis ( $n = 9$ ). The remaining 2,074 patients were included in the study, and their characteristics were shown in Table 3.1 (first column). The unadjusted and adjusted association between patient variables and each indicator of aggressive EOL care are shown in Table 3.1 and Table 3.2, respectively.

#### 3.3.1 Chemotherapy

In total, 30.3% of patients ( $n = 628$ ) received chemotherapy in the last 6 months of life; 3.7% ( $n = 76$ ) received chemotherapy in the last 14 days of life. In unadjusted analyses, the proportion of patients receiving chemotherapy in the last 14 days was highest for patients aged  $\leq 60$  years. Patients with shorter durations of disease and stage IV cancer were more likely to receive chemotherapy in the last 14 days (Table 3.1). In the adjusted analysis, only age had statistically significant association. With age increasing, odds of receiving chemotherapy in the last 14 days decreased. Compared with patients aged  $\leq 60$  years, the adjusted odds ratios of receiving chemotherapy in the last 14 days for patients aged 71-80 and over 80 years were 0.41 (95% CI: 0.22, 0.77) and 0.05 (95% CI: 0.01, 0.24), respectively. (Table 3.2)

### 3.3.2 *ER Visit*

In total, 76% (n = 1,577) of patients had visited ER during the last six months of life. In the last 30 days of life, 42% (n = 873) of patients had at least one ER visit and 12.5% (n = 259) had more than one ER visit. Patients who lived in Northern Alberta had the highest proportion of having more than one ER visit in the last 30 days life (25.4%). Patient who had chemotherapy during the last 6 months of life and patients aged 61-70 years also had a higher proportion of having more than one ER visit in the last 30 days life (Table 3.1). In both unadjusted and adjusted analyses, male, living in rural region, higher level of comorbidity, having follow-up visit with oncologist, and receiving chemotherapy in the last 6 months were associated with increased odds of having at least one ER visit in the last 30 days. Compared with patients who lived in Calgary, patients lived in three rural regions (North, Central, and South) had 2-4 times of adjusted odds of having more than one ER visit in the last 30 days of life. (Table 3.2)

### 3.3.3 *Hospital Admission*

In total, 81.1% (n = 1,683) of patients had hospital admission in the last six months of life. Of the total 3,388 admissions, 92.4% were to acute care hospitals. The average and median length of hospital stay were 32.2 and 22 days, respectively. There were 9.5% (n = 198) of patients who had more than one hospital admission in their last 30 days of life; the average and median length of stay were 14.8 and 14 days, respectively. Patients who lived in Northern and Southern Alberta had the highest proportions of having one or more hospital admission.

In both unadjusted and adjusted analyses, being male, living in Edmonton and three rural regions, presence of one or more co-morbidity, having follow-up visit to oncologist were

associated with having multiple hospitalization in the last 30 days of life. Compared with patients who lived in Calgary, patients who lived in other four regions had 3.3 to 5.3 times of adjusted odds of having more than one hospitalization in the last 30 days of life. Age and chemotherapy use were not significantly associated with having more than one hospitalization in the adjusted analysis. (Table 3.2)

#### *3.3.4 ICU Admission*

In total, 2.2% (n = 46) of patients were admitted to ICU in the last 30 days of life; of them 38 died in the ICU. Patients with stage I or II CRC had the highest proportion of ICU admission. Region of residence, cancer stage, duration of disease and comorbidity had significant associations with ICU admission in the last 30 days of life, in both unadjusted and adjusted analyses. Adjusted odds of being admitted to ICU in the last 30 days for patients who survived 6-18 months, 18-36 months and over three years were 0.25, 0.18 and 0.09 times, respectively, of that for patients survived 1-6 months. Patients with comorbidity index of two or more had 2.5 times odds of having ICU admission compared with patients without any comorbidity. Patients with stage I/II cancer and with stage III cancer had 9.1 and 5.5 times odds of having ICU admission in the last 30 days, compared with patients with stage IV cancer. (Table 3.2)

#### *3.3.5 Death in Acute Care Hospital*

Half (50.1%, n = 1,039) of patients died in acute care hospital. The mean and median length of stay for their terminal admission were 20.1 and 11 days, respectively. Of all deaths in acute care hospital, 22.4% (n = 233) occurred within three days of terminal admission and 40.2% (n = 418)

occurred within seven days of admission. The proportion of in-hospital death varied by region from 33.7% in Calgary to 77.6% Northern Alberta.

In both unadjusted and adjusted analyses, male, younger age, living in rural regions, higher comorbidity, having consultation or follow-up visit with oncologist, and receiving chemotherapy were positively associated with death in acute care hospital. All cancer-specific variables (i.e., site, stage, duration, and history of other cancer) were not associated with death in acute care hospital.

### *3.3.6 Composite Measure of Indicators*

Overall, 44.5% of patients had no indicator of aggressive EOL care, 38.7% had one indicator, and 16.8% had two or more indicators (including 11.7% had two indicators, 4.8% had three, 0.3% had four, and 0.05% had five). Table 3.3 shows the results of unadjusted and adjusted analyses for the composite measure of aggressive care. In both unadjusted and adjusted analyses, being male, younger age, rural residence, comorbidity, having follow-up visit to oncologist, and receiving chemotherapy in the last 6 months were positively associated with having one and having two or more indicators of aggressive EOL care. Duration of disease, consult with oncologist and radiotherapy use had no significant association with any number of indicators in unadjusted analysis but appeared significant in adjusted analysis. Consult with oncologist increased the odds of having one or more indicators, whereas receiving radiotherapy decreased the odds of having one or more indicators. Increased duration of the disease was associated with decreased odds of having two or more indicators.

Adjusted odds of having two or more indicators for male was twice of that for female. Odds of having two or more indicators for patients who received chemotherapy was three times of that for patient who did not. Odds of having two or more indicator for patients aged above 80 years was less than half (0.45) of that for patients under 60. For patients with comorbidity index of two or more, adjusted odds of having one indicator and two or more indicators were 2.7 times and 3.4 times, respectively, of that for patients without comorbidity. Compared with patients who lived in Calgary, patients in Southern Alberta had 3.1 times and 3.5 times, patients in Central Alberta had 6.5 times and 5.2 times, and patients in Northern Alberta had 8.9 times and 12.2 times, adjusted odds of having one and two or more indicators of aggressive EOL care, respectively.

### **3.4 Discussion**

In this study, we examined utilization of acute care at the EOL period among patients who died of CRC in Alberta, Canada in the years 2006-2009. Five quality indicators for EOL cancer care, i.e., proportions of chemotherapy use, ER visit, hospitalization, and ICU admission at the specific EOL periods, as well as death in an acute care hospital were measured. We examined patient demographic/clinical characteristics as well as oncology care received to determine their association with the indicators. Associations between patient variables and the extent of aggressive EOL care were also assessed.

Similar to previous studies,<sup>6, 7, 10, 15, 28, 29,30</sup> we found that male, younger age, earlier tumor stage, shorter survival after diagnosis, presence of co-morbidity, and living in rural area were related to more aggressive care. In contrast to studies that demonstrated time trend towards more aggressive of EOL cancer care,<sup>6, 10</sup> no consistent temporal trend was observed in our data for

each indicator or their composite. Tumor site or whether having other cancer was also not associated with any indicator and their composite.

Striking variation by region was observed for indicators of ER visit, hospitalization, ICU admission and in-hospital death. Three less-populated and rural regions (Northern, Central, and Southern Alberta) had higher proportions of patients using aggressive EOL care and dying in hospital, compared with those in urban areas (Calgary and Edmonton). Residents in Northern Alberta (the most remote area) were most likely to use hospital care at the end of life. By contrast, residents in Calgary were least likely to use hospital care services. The variation across regions in acute care utilization at the end of life may be related to differences in the regional care protocol or geographic variation in availability of health care resources. Non-hospital-based supportive care services and facilities (e.g., long-term beds, home care, or palliative care services) were extensively available in urban centers, compared to smaller communities in which these types of services would only be available at local hospitals.<sup>31, 32</sup> On the other hand, differences in patient awareness of availability of health services may also contribute to the regional variation. The geographical disparity suggests the need for further investigation and potential intervention for system improvement for equitable access to appropriate EOL cancer care.

Interestingly, there was an association between oncology service variables and certain indicators of aggressive EOL care. For example, having a follow-up visit with an oncologist was associated with more ER visits, hospitalizations, and in-hospital deaths. Similarly, having chemotherapy in the last six months of life was associated with increased ER visits, ICU admissions and in-

hospital deaths. Having radiotherapy, however, was related to decreased deaths in acute care hospital. The association between chemotherapy use and more acute care use may be due to adverse effects of chemotherapy that might cause more acute care needs. The negative association between radiotherapy use and death in acute care hospital may be explained by the palliative role of radiotherapy, particularly in symptom palliation for cancer patients near the end of life.<sup>33</sup> The positive association between follow-up visit with an oncologist and more aggressive care, especially for hospitalization, is surprising. Further investigation is required to identify the underlying reason for this association.

Table 3.4 summarizes results from previous studies that measured quality indicators of EOL cancer care. Due to different cancer type, results from our study are not directly comparable with the results of other studies. However, our results are in line with results from Ontario, Canada. The proportion for deaths in an acute care hospital in our study compares favorably against other provinces in Canada, especially those with reported rates 60% or higher. A study in Ontario reported 22.4% of cancer decedents in 1993-2004 experienced at least one of the four indicators of aggressive care excluding death in an acute care hospital,<sup>10</sup> the corresponding figure in our study is 21.5%. Results from an Ontario study showed that of CRC decedents in 2001, 11.3% received chemotherapy and 8% had ICU admission in the last 14 days of life,<sup>34</sup> the proportion in our study is 3.7% and 1.2%. However, compared with benchmarks set by Earle *et al.* based on U.S. SEER data<sup>17</sup> and results of another U.S. study,<sup>6</sup> our results are much higher in proportions of death in acute care hospital, ER visit and hospitalization, but lower in chemotherapy use and ICU admission. Differences in characteristics of healthcare systems between the two countries,

e.g., publicly versus privately funded systems, different level of availability of hospice, financial incentive for drug prescription, may explain the disparity observed.

This study is the first study in Alberta that assessed EOL cancer care in the province-wide population-based manner. It has used a sound methodology to obtain and link data from different data sources and demonstrated that these indicators are measurable and feasible using administrative data in Alberta. Using CRC as a starting point, the methods can be expanded to other cancer deaths. Given the trend towards using population-based indicators to measure quality of cancer care, the quality indicators can be continuously measured and serve as a surveillance tool, to help identify opportunities for quality improvement.

Our study has several limitations. First, the quality indicators we measured mainly focus on aggressive acute care. Palliative care, including hospice or home care, was not examined in this study because of unavailability of provincial-level data on palliative care. Indicators for ER use and/or hospital admission, however, are indirect measures of a lack of these services. In the future, we hope to add data on palliative care and home care use. Second, we relied on administrative data sources to identify services the patient use, which have not been validated with chart review. For example, ER visits to hospitals, especially to those in rural communities, are possible for scheduled appointment rather than urgent care-seeking, hence the number of ER visits as aggressive EOL care tend to be overestimated. Also, using death certificate to identify cause of death can be problematic, especially for patients with other conditions that potentially cause death, although this is a common practice for identifying individuals who died of cancer.<sup>35</sup> Finally, indicators used in this study do not represent complete ranges of quality in EOL care.

Absence of these indicators does not imply good quality of care, and having indicators does not necessarily mean that patient received inappropriate care. For instance, 75% of patients who received chemotherapy in their last 14 days of life had stage IV disease, for which chemotherapy might be given for palliation. Also, for patients who died in an acute care hospital, a considerable proportion died within few days of admission, potentially suggesting that dying in hospital might be their personal choice.

### **3.5 Conclusion**

The findings from this study can serve as baseline information for future comparison on EOL cancer care. They can also serve for hypothesis-generation for following research and intervention. The results indicate that healthcare within a large integrated system has substantial geographic variation in EOL care for CRC patients, which warrant potential intervention to eliminate disparities by region and to ensure equality of access to healthcare services.

### **3.6 Acknowledgement**

This research was funded by Alberta Cancer Foundation. The authors would thank John Fleming, Cancer Care, Alberta Health Services, for his tremendous assistance in data preparation and validation. None of the authors has a conflict of interest.

**Table 3.1 Characteristics of patients who died of CRC in Alberta in 2006-2009, and association with end-of-life quality care indicators**

Characteristics	Number (%) of Patients					
	Total	Chemotherapy in the last 14 days*	>1 ER visit in the last 30 days*	>1 hospitalization in the last 30 days*	ICU admission in the last 30 days*	Death in an acute care hospital*
<b>Total</b>	2074 (100)	76 (3.7)	259 (12.5)	198 (9.5)	46 (2.2)	1039 (50.1)
<b>Sex</b>		<i>P</i> = .07	<i>P</i> < .001	<i>P</i> = .002	<i>P</i> = .19	<i>P</i> < .0001
Female	918 (44.3)	26 (2.8)	88 (9.6)	67 (7.3)	16 (1.7)	412 (44.9)
Male	1156 (55.7)	50 (4.3)	171 (14.8)	131 (11.3)	30 (2.6)	627 (54.2)
<b>Age at death, yrs  </b>		<i>P</i> < .0001	<i>P</i> = .002	<i>P</i> = .0003	<i>P</i> = .38	<i>P</i> < .0001
Median [Range]	71 [24, 100]	63.5 [32, 83]	69 [35, 100]	67.7 [34, 97]	76 [44, 93]	71 [24, 100]
≤60	451 (21.7)	32 (7.1)	60 (13.3)	54 (12.0)	8 (1.8)	250 (55.4)
61-70	471 (22.7)	24 (5.1)	83 (17.6)	55 (11.7)	8 (1.7)	258 (54.8)
71-80	611 (29.5)	18 (2.9)	69 (11.3)	58 (9.5)	18 (2.9)	306 (50.1)
>80	541 (26.1)	2 (0.4)	47 (8.7)	31 (5.7)	12 (2.2)	225 (41.6)
<b>Year of death</b>		<i>P</i> = .34	<i>P</i> = .23	<i>P</i> = .87	<i>P</i> = .88	<i>P</i> = .01
2006	507 (24.4)	22 (4.3)	53 (10.5)	46 (9.1)	11 (2.2)	254 (50.1)
2007	535 (25.8)	20 (3.7)	65 (12.1)	55 (10.3)	13 (2.4)	294 (55.0)
2008	502 (24.2)	12 (2.4)	74 (14.7)	45 (9.0)	9 (1.8)	224 (44.6)
2009	530 (25.6)	22 (4.2)	67 (12.6)	52 (9.8)	13 (2.5)	267 (50.4)
<b>Region of residence at death</b>		<i>P</i> = .14	<i>P</i> < .0001	<i>P</i> < .0001	<i>P</i> = .008	<i>P</i> < .0001
Edmonton	670 (32.3)	17 (2.5)	77 (11.5)	74 (11.0)	8 (1.2)	286 (42.7)
Calgary	629 (30.3)	29 (4.6)	47 (7.5)	23 (3.7)	14 (2.2)	212 (33.7)
Northern	232 (11.2)	5 (2.2)	59 (25.4)	38 (16.4)	8 (3.4)	180 (77.6)
Central	355 (17.1)	17 (4.8)	50 (14.1)	39 (11.0)	6 (1.7)	254 (71.5)
Southern	188 (9.1)	8 (4.3)	26 (13.8)	24 (12.8)	10 (5.3)	107 (56.9)

<b>Tumor site</b>		<i>P</i> = .9	<i>P</i> = .26	<i>P</i> = .97	<i>P</i> = .2	<i>P</i> = .8
Colon	1286 (62.0)	47 (3.7)	163 (12.7)	122 (9.5)	27 (2.1)	650 (50.5)
Rectum	572 (27.6)	20 (3.5)	63 (11.0)	56 (9.8)	17 (3.0)	285 (49.8)
Rectosigmoid	216 (10.4)	9 (4.2)	33 (15.3)	20 (9.3)	2 (0.9)	104 (48.1)
<b>Stage at diagnosis</b>		<i>P</i> < .001	<i>P</i> = .31	<i>P</i> = .90	<i>P</i> < .0001	<i>P</i> = .12
I/II	295 (14.2)	7 (2.4)	35 (11.9)	28 (9.5)	17 (5.8)	158 (53.6)
III	459 (22.1)	10 (2.2)	50 (10.9)	48 (10.5)	15 (3.3)	239 (52.1)
IV	1075 (51.8)	57 (5.3)	148 (13.8)	99 (9.2)	11 (1.0)	534 (49.7)
Missing †	245 (11.8)	2 (0.8)	26 (10.6)	23 (9.4)	3 (1.2)	108 (44.1)
<b>Duration of disease, months  </b>		<i>P</i> = .004	<i>P</i> = .45	<i>P</i> = .52	<i>P</i> = .003	<i>P</i> = .82
Median [Range]	17.2 [1, 550]	11.7 [1, 81.2]	15.8 [1, 266.2]	27.7 [1, 266.2]	7.1[1.1, 105.3]	16.4 [1, 383.5]
1-6	471 (22.7)	27 (5.7)	60 (12.7)	43 (9.1)	21 (4.5)	231 (49.0)
6-18	607 (29.3)	20 (3.3)	84 (13.8)	68 (11.2)	10 (1.6)	319 (52.6)
18-36	492 (23.7)	20 (4.1)	54 (11.0)	42 (8.5)	8 (1.6)	237 (48.2)
>36	504 (24.3)	9 (1.8)	61 (12.1)	45 (8.9)	7 (1.4)	252 (50.0)
<b>Charlson Comorbidity index  </b>		<i>P</i> = .71	<i>P</i> = .001	<i>P</i> < .0001	<i>P</i> < .0001	<i>P</i> < .0001
0	1061 (51.2)	41 (3.9)	106 (10.0)	79 (7.4)	13 (1.2)	452 (42.6)
1	435 (21.0)	9 (2.1)	65 (14.9)	41 (9.4)	8 (1.8)	223 (51.3)
≥2	578 (27.9)	26 (4.5)	88 (15.2)	78 (13.5)	25 (4.3)	364 (63.0)
<b>Other cancer</b>		<i>P</i> = .18	<i>P</i> = .92	<i>P</i> = .55	<i>P</i> = .12	<i>P</i> = .09
No	1556 (75.0)	62 (4.0)	195 (12.5)	152 (9.8)	39 (2.5)	796 (51.2)
Yes	518 (25.0)	14 (2.7)	64 (12.4)	46 (8.9)	7 (1.4)	243 (46.9)
<b>Consult with oncologist in the last 6 months †</b>			<i>P</i> = .32	<i>P</i> = .01	<i>P</i> = .11	<i>P</i> = .24
No	1448 (69.8)	-	174 (12.0)	123 (8.5)	37 (2.6)	713 (49.2)
Yes	626 (30.2)	-	85 (13.6)	75 (12.0)	9 (1.4)	326 (52.1)
<b>Follow-up visit with oncologist in the last 6 months †</b>			<i>P</i> < .0001	<i>P</i> < .0001	<i>P</i> = .04	<i>P</i> < .0001

No	907 (43.7)	-	76 (8.4)	53 (5.8)	27 (3.0)	398 (43.9)
Yes	1167 (56.3)	-	183 (15.7)	145 (12.4)	19 (1.6)	641 (54.9)
<b>Radiotherapy in the last 6 months †</b>			<i>P</i> = .91	<i>P</i> = .06	<i>P</i> = .08	<i>P</i> = .48
No	1749 (84.3)	-	219 (12.5)	158 (9.0)	43 (2.5)	882 (50.4)
Yes	325 (15.7)	-	40 (12.3)	40 (12.3)	3 (0.9)	157 (48.3)
<b>Chemotherapy in the last 6 months †</b>			<i>P</i> < .0001	<i>P</i> = .002	<i>P</i> = .98	<i>P</i> < .0001
No	1446 (69.7)	-	137 (9.5)	119 (8.2)	32 (2.2)	658 (45.5)
Yes	628 (30.3)	-	122 (19.4)	79 (12.6)	14 (2.2)	381 (60.7)

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\* Percentages are row percentages, denominators is the row-specific number for the entire cohort

| P-values were calculated by Cochran-Armitage trend test.

† This category includes 45 patients with a cancer histology that could not be staged and 200 patients whose staging data were not available.

‡ Variable not included in analysis for outcomes of chemotherapy use because such association is not meaningful.

**Table 3.2** Logistic regression for indicators of aggressive care

Characteristics	Odds Ratio (95% Confidence Interval)				
	Chemotherapy in the last 14 days	>1 ER visits in the last 30 days of life	>1 hospitalization in the last 30 days	ICU admission in the last 30 days	Death in acute care hospital
<b>Sex</b>	<i>P</i> = .31	<i>P</i> = <b>.001</b>	<i>P</i> = <b>.005</b>	<i>P</i> = .42	<i>P</i> < <b>.001</b>
Female	ref	ref	ref	ref	ref
Male	1.30 (0.78 - 2.15)	1.61 (1.20 - 2.15)	1.60 (1.16 - 2.21)	1.31 (0.68 - 2.54)	1.43 (1.17 - 1.74)
<b>Age at death</b>	<i>P</i> = <b>.0003</b>	<i>P</i> = .21	<i>P</i> = .13	<i>P</i> = .58	<i>P</i> = <b>.04</b>
≤60	ref	ref	ref	ref	ref
61-70	0.67 (0.38 - 1.18)	1.25 (0.85 - 1.83)	0.87 (0.57 - 1.32)	0.75 (0.27 - 2.13)	0.83 (0.62 - 1.11)
71-80	0.41 (0.22 - 0.77)	0.86 (0.57 - 1.29)	0.73 (0.47 - 1.13)	1.09 (0.42 - 2.86)	0.72 (0.54 - 0.96)
>80	0.05 (0.01 - 0.24)	0.87 (0.53 - 1.42)	0.52 (0.30 - 0.91)	0.63 (0.21 - 1.93)	0.63 (0.45 - 0.87)
<b>Year of death</b>	<i>P</i> = .27	<i>P</i> = .12	<i>P</i> = .91	<i>P</i> = .99	<i>P</i> = <b>.01</b>
2006	ref	ref	ref	ref	ref
2007	0.83 (0.44 - 1.57)	1.15 (0.77 - 1.72)	1.14 (0.74 - 1.74)	0.98 (0.41 - 2.35)	1.16 (0.88 - 1.52)
2008	0.51 (0.24 - 1.05)	1.58 (1.07 - 2.34)	0.99 (0.63 - 1.54)	0.93 (0.37 - 2.36)	0.74 (0.56 - 0.97)
2009	0.98 (0.53 - 1.83)	1.16 (0.78 - 1.72)	1.01 (0.65 - 1.56)	1.02 (0.43 - 2.43)	0.98 (0.75 - 1.28)
<b>Region of residence at death</b>	<i>P</i> = .07	<i>P</i> < <b>.0001</b>	<i>P</i> < <b>.0001</b>	<i>P</i> = <b>.04</b>	<i>P</i> < <b>.0001</b>
Calgary	ref	ref	ref	ref	ref
Edmonton	0.53 (0.28 - 1.00)	1.64 (1.11 - 2.43)	3.32 (2.03 - 5.43)	0.43 (0.17 - 1.07)	1.45 (1.14 - 1.85)
North	0.44 (0.17 - 1.17)	4.34 (2.80 - 6.72)	5.29 (3.02 - 9.25)	1.13 (0.43 - 2.94)	7.75 (5.36 - 11.20)
Central	1.23 (0.65 - 2.32)	2.00 (1.29 - 3.09)	3.49 (2.01 - 6.04)	0.51 (0.19 - 1.42)	5.60 (4.14 - 7.58)
South	1.09 (0.48 - 2.48)	2.01 (1.18 - 3.41)	4.12 (2.22 - 7.64)	1.87 (0.75 - 4.65)	2.78 (1.95 - 3.97)
<b>Tumor site</b>	<i>P</i> = .95	<i>P</i> = .19	<i>P</i> = .75	<i>P</i> = .23	<i>P</i> = .40
Colon	ref	ref	ref	ref	ref
Rectum	0.99 (0.56 - 1.72)	0.79 (0.57 - 1.10)	0.88 (0.62 - 1.26)	1.51 (0.77 - 2.99)	0.90 (0.72 - 1.13)
Rectosigmoid	1.12 (0.53 - 2.38)	1.20 (0.78 - 1.84)	0.88 (0.53 - 1.47)	0.45 (0.10 - 2.03)	0.83 (0.60 - 1.14)

<b>Stage at diagnosis</b>	<i>P</i> = .35	<i>P</i> = .69	<i>P</i> = .21	<i>P</i> < .0001	<i>P</i> = .14
IV	ref	ref	ref	ref	ref
I/II	0.74 (0.31 - 1.75)	1.09 (0.69 - 1.71)	1.47 (0.89 - 2.42)	9.07 (3.63 - 22.63)	1.29 (0.95 - 1.76)
III	0.59 (0.28 - 1.23)	0.84 (0.57 - 1.23)	1.34 (0.89 - 2.00)	5.54 (2.31 - 13.29)	1.15 (0.88 - 1.49)
Missing	0.38 (0.09 - 1.67)	1.08 (0.64 - 1.82)	1.70 (0.96 - 3.01)	1.88 (0.46 - 7.80)	0.86 (0.61 - 1.23)
<b>Duration of disease</b>	<i>P</i> = .06	<i>P</i> = .54	<i>P</i> = .56	<i>P</i> < .0001	<i>P</i> = .96
1-6 months	ref	ref	ref	ref	ref
6-18 months	0.51 (0.28 - 0.95)	0.85 (0.57 - 1.28)	1.03 (0.65 - 1.61)	0.26 (0.11 - 0.62)	1.04 (0.78 - 1.39)
18-36 months	0.65 (0.34 - 1.22)	0.71 (0.45 - 1.12)	0.83 (0.50 - 1.39)	0.20 (0.07 - 0.51)	0.97 (0.71 - 1.32)
>36 months	0.36 (0.16 - 0.85)	0.82 (0.51 - 1.32)	0.76 (0.45 - 1.30)	0.11 (0.04 - 0.32)	1.02 (0.74 - 1.41)
<b>Charlson Comorbidity</b>	<i>P</i> = .10	<i>P</i> = .001	<i>P</i> = .003	<i>P</i> = .04	<i>P</i> < .0001
0	ref	ref	ref	ref	ref
1	0.68 (0.32 - 1.45)	1.73 (1.21 - 2.46)	1.32 (0.87 - 2.00)	1.29 (0.51 - 3.26)	1.61 (1.25 - 2.07)
≥2	1.52 (0.89 - 2.60)	1.65 (1.19 - 2.28)	1.84 (1.29 - 2.61)	2.54 (1.21 - 5.33)	2.58 (2.04 - 3.27)
<b>Other cancer</b>	<i>P</i> = .96	<i>P</i> = .40	<i>P</i> = .72	<i>P</i> = .09	<i>P</i> = .85
No	ref	ref	ref	ref	ref
Yes	1.02 (0.54 - 1.90)	1.15 (0.83 - 1.60)	1.07 (0.74 - 1.55)	0.47 (0.20 - 1.11)	0.98 (0.78 - 1.23)
<b>Consult with oncologist in the last 6 months</b>		<i>P</i> = .61	<i>P</i> = .15	<i>P</i> = .17	<i>P</i> = .03
No		ref	ref	ref	ref
Yes	-	1.09 (0.78 - 1.53)	1.31 (0.91 - 1.90)	0.55 (0.23 - 1.28)	1.31 (1.02 - 1.67)
<b>Follow-up visit with oncologist in the last 6 months</b>		<i>P</i> = .01	<i>P</i> < .001	<i>P</i> = .32	<i>P</i> = .02
No		ref	ref	ref	ref
Yes	-	1.66 (1.11 - 2.47)	2.23 (1.44 - 3.45)	0.61 (0.23 - 1.60)	1.38 (1.06 - 1.80)
<b>Radiotherapy in the last 6 months</b>		<i>P</i> = .12	<i>P</i> = .62	<i>P</i> = .39	<i>P</i> = .02

No		ref	ref	ref	ref
Yes	-	0.72 (0.48 - 1.09)	0.90 (0.58 - 1.38)	0.56 (0.15 - 2.08)	0.71 (0.53 - 0.95)
<b>Chemotherapy in the last 6 months</b>		<b><i>P</i> = .001</b>	<b><i>P</i> = .98</b>	<b><i>P</i> = .04</b>	<b><i>P</i> = .005</b>
No		ref	ref	ref	ref
Yes	-	1.80 (1.27 - 2.54)	1.00 (0.69 - 1.45)	2.80 (1.07 - 7.37)	1.45 (1.12 - 1.87)

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ref: reference group

**Table 3.3 Factors related to having one or more than one indicator of aggressive care**

Characteristics	Unadjusted analysis N (%*)			P	Adjusted analysis OR (95% CI)		P
	Had no indicator (N = 922)	Had 1 indicator (N = 802)	Had ≥2 indicators (N = 350)		Had 1 indicator	Had ≥2 indicators	
<b>Sex</b>							
female	459 (50.0)	344 (37.5)	115 (12.5)	<b>&lt;.0001</b>	ref	ref	<b>&lt;.0001</b>
male	463 (40.1)	458 (39.6)	235 (20.3)		1.30 (1.05 - 1.61)	1.95 (1.46 - 2.60)	
<b>Age at death</b>							
≤60	174 (38.6)	181 (40.1)	96 (21.3)	<b>&lt;.0001</b>	ref	ref	<b>0.03</b>
61-70	177 (37.6)	193 (41.0)	101 (21.4)		0.92 (0.67 - 1.26)	0.87 (0.59 - 1.28)	
71-80	277 (45.3)	233 (38.1)	101 (16.5)		0.71 (0.52 - 0.97)	0.64 (0.43 - 0.95)	
>80	294 (54.3)	195 (36.0)	52 (9.6)		0.68 (0.48 - 0.96)	0.45 (0.28 - 0.73)	
<b>Year of death</b>							
2006	229 (45.2)	199 (39.3)	79 (15.6)	0.52	ref	ref	0.72
2007	221 (41.3)	213 (39.8)	101 (18.9)		1.06 (0.79 - 1.42)	1.24 (0.85 - 1.82)	
2008	238 (47.4)	186 (37.1)	78 (15.5)		0.84 (0.63 - 1.14)	0.95 (0.64 - 1.41)	
2009	234 (44.2)	204 (38.5)	92 (17.4)		0.98 (0.73 - 1.31)	1.04 (0.71 - 1.53)	
<b>Region of residence at death</b>							
Calgary	395 (62.8)	162 (25.8)	72 (11.4)	<b>&lt;.0001</b>	ref	ref	<b>&lt;.0001</b>
Edmonton	331 (49.4)	240 (35.8)	99 (14.8)		1.83 (1.41 - 2.38)	1.74 (1.21 - 2.50)	
North	40 (17.2)	121 (52.2)	71 (30.6)		8.94 (5.88 - 13.59)	12.25 (7.45 - 20.15)	
Central	87 (24.5)	199 (56.1)	69 (19.4)		6.52 (4.69 - 9.06)	5.15 (3.32 - 7.97)	
South	69 (36.7)	80 (42.6)	39 (20.7)		3.14 (2.13 - 4.64)	3.53 (2.12 - 5.86)	
<b>Tumor site</b>							
Colon	571 (44.4)	501 (39.0)	214 (16.6)	0.97	ref	ref	0.87
Rectum	253 (44.2)	222 (38.8)	97 (17.0)		0.98 (0.77 - 1.26)	0.91 (0.66 - 1.26)	
Rectosigmoid	98 (45.4)	79 (36.6)	39 (18.1)		0.85 (0.60 - 1.20)	0.94 (0.60 - 1.47)	

<b>Stage at diagnosis</b>							
IV	469 (43.6)	419 (39.0)	187 (17.4)	0.19	ref	ref	0.06
I/II	121 (41.0)	119 (40.3)	55 (18.6)		1.17 (0.83 - 1.64)	1.84 (1.18 - 2.85)	
III	204 (44.4)	178 (38.8)	77 (16.8)		0.98 (0.74 - 1.30)	1.25 (0.87 - 1.82)	
Missing	128 (52.2)	86 (35.1)	31 (12.7)		0.73 (0.50 - 1.07)	1.08 (0.64 - 1.84)	
<b>Time from diagnosis to death</b>							
1-6 months	208 (44.2)	172 (36.5)	91 (19.3)	0.37	ref	ref	<b>0.03</b>
6-18 months	253 (41.7)	248 (40.9)	106 (17.5)		1.11 (0.81 - 1.51)	0.63 (0.42 - 0.94)	
18-36 months	230 (46.7)	189 (38.4)	73 (14.8)		1.06 (0.76 - 1.49)	0.51 (0.33 - 0.80)	
>36 months	231 (45.8)	193 (38.3)	80 (15.9)		1.09 (0.77 - 1.55)	0.55 (0.35 - 0.87)	
<b>Charlson comorbidity index</b>							
0	556 (52.4)	358 (33.7)	147 (13.9)	<b>&lt;.0001</b>	ref	ref	<b>&lt;.0001</b>
1	187 (43.0)	179 (41.1)	69 (15.9)		1.72 (1.31 - 2.26)	1.69 (1.17 - 2.45)	
≥2	179 (31.0)	265 (45.8)	134 (23.2)		2.66 (2.06 - 3.44)	3.44 (2.48 - 4.76)	
<b>Other cancer</b>							
No	683 (43.9)	597 (38.4)	276 (17.7)	0.19	ref	ref	0.48
Yes	239 (46.1)	205 (39.6)	74 (14.3)		1.15 (0.90 - 1.47)	1.01 (0.72 - 1.42)	
<b>Consult with oncologist in the last 6 months</b>							
No	665 (45.9)	553 (38.2)	230 (15.9)	0.07	ref	ref	<b>0.02</b>
Yes	257 (41.1)	249 (39.8)	120 (19.2)		1.47 (1.13 - 1.92)	1.29 (0.92 - 1.82)	
<b>Follow-up care by oncologist in the last 6 months</b>							
No	473 (52.1)	332 (36.6)	102 (11.2)	<b>&lt;.0001</b>	ref	ref	<b>0.006</b>
Yes	449 (38.5)	470 (40.3)	248 (21.3)		1.44 (1.09 - 1.91)	1.76 (1.19 - 2.61)	

**Radiotherapy  
in the last 6  
months**

No	771 (44.1)	689 (39.4)	289 (16.5)	0.26	ref	ref	<b>0.006</b>
Yes	151 (46.5)	113 (34.8)	61 (18.8)		0.59 (0.43 - 0.82)	0.68 (0.45 - 1.02)	

**Chemotherapy  
in the last 6  
months**

No	725 (50.1)	547 (37.8)	174 (12.0)	<b>&lt;.0001</b>	ref	ref	<b>&lt;.0001</b>
Yes	197 (31.4)	255 (40.6)	176 (28.0)		1.37 (1.03 - 1.82)	3.02 (2.11 - 4.32)	

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\*percentages are row percentages

**Table 3.4**      **Reported findings of quality indicators for end of life cancer care in the U.S. and Canada**

<b>Study</b>	<b>Cancer type</b>	<b>Chemotherapy in the last 14 days of life</b>	<b>&gt;1 ER visit in the last month of life</b>	<b>&gt;1 hospital admission in the last month of life</b>	<b>ICU admission in the last month of life</b>	<b>Death in an acute care hospital</b>
<b>Benchmark (U.S.)<sup>17</sup>§</b>	<b>All</b>	<b>10%</b>	<b>4%</b>	<b>4%</b>	<b>4%</b>	<b>17%</b>
U.S. 1993-1996 <sup>6</sup> †	All	15.6%	8.5%	8.5%	10.6%	30.7%
Ontario 1993-2004 <sup>10</sup> ‡	All	2.02-2.88%	8.6-10.53%	7.5-8.5%	3.06-5.39%	—
Ontario 2001 <sup>7, 36</sup>	All	4.2%	27.6%*	-	5.4%*	56%
Ontario 2000-2004 <sup>15</sup>	All	-	-	-	-	55%
Nova Scotia 1992-1997 <sup>29</sup>	All	-	-	-	-	73.0%
Ontario 1998-2002 <sup>18</sup>	Breast	6.4%	6.9%	15.6%	4.1%	52.9%
Nova Scotia 1998-2002 <sup>18</sup>	Breast	2.4%	5.6%	11.7%	2.1%	63.4%
Quebec 1992-1998 <sup>37</sup>	Breast	-	-	-	-	69.6%
<b>Alberta 2006-2009</b>	<b>CRC</b>	<b>3.7%</b>	<b>12.5%</b>	<b>9.5%</b>	<b>2.2%</b>	<b>50.1%</b>

§ Proposed by Earle et al, based on Surveillance, Epidemiology and End Results (SEER)-Medicare data for 48,906

US cancer decedents  $\geq$  65 years old in 1991-1996

† Based on SEER-Medicare data for cancer decedents  $\geq$  65 years old

‡ Results based on decedents  $\geq$  65 years old.

\* Based on the last two weeks of life.

CRC: colorectal cancer

**Appendix 3.1 Unadjusted and adjusted analysis for chemotherapy use in the last 6 months and last 30 days of life**

Characteristics	Chemotherapy in the last 6 months		Chemotherapy in the last 30 days	
	<i>N</i> (%)	OR (95% CI)	<i>N</i> (%)	OR (95% CI)
<b>Total</b>	<b>628 (30.3)</b>	—	<b>153 (7.4)</b>	—
<b>Sex</b>	<i>P</i> = .21	<i>P</i> = .99	<i>P</i> = <b>.003</b>	<i>P</i> = <b>.01</b>
Female	265 (28.9)	ref	50 (5.4)	ref
Male	363 (31.4)	1.00 (0.80 - 1.25)	103 (8.9)	1.59 (1.09 - 2.30)
<b>Age at death, yrs</b>	<i>P</i> < <b>.0001</b>	<i>P</i> < <b>.0001</b>	<i>P</i> < <b>.0001</b>	<i>P</i> < <b>.0001</b>
≤60	225 (49.9)	ref	60 (13.3)	ref
61-70	216 (45.9)	0.89 (0.68 - 1.18)	51 (10.8)	0.75 (0.49 - 1.13)
71-80	153 (25.0)	0.39 (0.29 - 0.52)	36 (5.9)	0.42 (0.26 - 0.67)
>80	34 (6.3)	0.09 (0.06 - 0.14)	6 (1.1)	0.08 (0.03 - 0.20)
<b>Year of death</b>	<i>P</i> = <b>.02</b>	<i>P</i> = <b>.008</b>	<i>P</i> = .08	<i>P</i> = <b>.05</b>
2006	149 (29.4)	ref	45 (8.9)	ref
2007	172 (32.1)	1.05 (0.78 - 1.42)	36 (6.7)	0.73 (0.46 - 1.18)
2008	127 (25.3)	0.75 (0.55 - 1.03)	26 (5.2)	0.54 (0.32 - 0.91)
2009	180 (34.0)	1.28 (0.95 - 1.73)	46 (8.7)	1.05 (0.67 - 1.64)
<b>Region of residence at death</b>	<i>P</i> = .07	<i>P</i> = <b>.0003</b>	<i>P</i> < <b>.001</b>	<i>P</i> < <b>.0001</b>
Calgary	183 (29.1)	ref	53 (8.4)	ref
Edmonton	183 (27.3)	0.87 (0.66 - 1.14)	29 (4.3)	0.47 (0.29 - 0.76)
Northern Alberta	73 (31.5)	1.12 (0.78 - 1.62)	11 (4.7)	0.52 (0.26 - 1.03)
Central Alberta	123 (34.6)	1.59 (1.16 - 2.20)	38 (10.7)	1.48 (0.93 - 2.34)
Southern Alberta	66 (35.1)	1.73 (1.16 - 2.59)	22 (11.7)	1.72 (0.99 - 2.99)
<b>Tumor site</b>	<i>P</i> = .47	<i>P</i> = .22	<i>P</i> = .93	<i>P</i> = .79
Colon	391 (30.4)	ref	97 (7.5)	ref
Rectum	165 (28.8)	0.80 (0.62 - 1.03)	41 (7.2)	0.88 (0.59 - 1.32)

Rectosigmoid	72 (33.3)	0.91 (0.65 - 1.29)	15 (6.9)	0.87 (0.49 - 1.57)
<b>Stage at diagnosis</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> = .21</b>
IV	426 (39.6)	ref	108 (10.0)	ref
I/II	52 (17.6)	0.37 (0.25 - 0.53)	13 (4.4)	0.64 (0.33 - 1.22)
III	129 (28.1)	0.55 (0.42 - 0.73)	26 (5.7)	0.72 (0.44 - 1.17)
Missing	21 (8.6)	0.21 (0.13 - 0.36)	6 (2.5)	0.47 (0.19 - 1.17)
<b>Duration of disease, months</b>	<b><i>P</i> = .005</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> = .01</b>	<b><i>P</i> = .34</b>
1-6	73 (15.5)	ref	40 (8.5)	ref
6-18	241 (39.7)	3.97 (2.86 - 5.50)	55 (9.1)	0.98 (0.63 - 1.54)
18-36	180 (36.6)	3.78 (2.67 - 5.35)	33 (6.7)	0.71 (0.42 - 1.19)
>36	134 (26.6)	3.51 (2.40 - 5.12)	25 (5.0)	0.67 (0.37 - 1.21)
<b>Charlson Comorbidity</b>	<b><i>P</i> = .002</b>	<b><i>P</i> = .16</b>	<b><i>P</i> = .60</b>	<b><i>P</i> = .69</b>
0	350 (33.0)	ref	84 (7.9)	ref
1	130 (29.9)	1.30 (0.98 - 1.73)	26 (6.0)	0.93 (0.58 - 1.51)
≥2	148 (25.6)	1.01 (0.77 - 1.31)	43 (7.4)	1.15 (0.77 - 1.74)
<b>Other cancer</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> = .22</b>	<b><i>P</i> = .02</b>	<b><i>P</i> = .53</b>
No	521 (33.5)	ref	127 (8.2)	ref
Yes	107 (20.7)	0.84 (0.64 - 1.11)	26 (5.0)	0.86 (0.54 - 1.37)

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OR: odds ratio; 95% CI: 95% confidence interval

**Appendix 3.2 Unadjusted and adjusted analysis for having more than one ER visit or hospitalization in the last 6 months**

Characteristics	>1 ER visit in the last 6 months		>1 hospitalization in the last 6 months	
	N (%)	OR (95% CI)	N (%)	OR (95% CI)
<b>Total</b>	<b>1017 (49.0)</b>	—	<b>930 (44.8)</b>	—
<b>N of admission</b>	<b>4135</b>	—	<b>2635</b>	—
<b>Mean [Median] total length of stay</b>	—	—	<b>41.7 [34]</b>	—
<b>Sex</b>	<i>P</i> = .18	<i>P</i> = .74	<i>P</i> = .16	<i>P</i> = .80
Female	435 (47.4)	ref	396 (43.1)	ref
Male	582 (50.3)	1.03 (0.85 - 1.25)	534 (46.2)	1.02 (0.85 - 1.24)
<b>Age at death, yrs</b>	<i>P</i> < .0001	<i>P</i> = .0002	<i>P</i> < .0001	<i>P</i> = .01
≤60	259 (57.4)	ref	232 (51.4)	ref
61-70	260 (55.2)	0.79 (0.60 - 1.05)	227 (48.2)	0.78 (0.59 - 1.03)
71-80	284 (46.5)	0.57 (0.43 - 0.76)	272 (44.5)	0.69 (0.52 - 0.91)
>80	214 (39.6)	0.53 (0.38 - 0.73)	199 (36.8)	0.59 (0.43 - 0.81)
<b>Year of death</b>	<i>P</i> = .93	<i>P</i> = .92	<i>P</i> = .82	<i>P</i> = .97
2006	244 (48.1)	ref	221 (43.6)	ref
2007	266 (49.7)	0.98 (0.76 - 1.28)	247 (46.2)	1.06 (0.81 - 1.37)
2008	250 (49.8)	1.04 (0.79 - 1.36)	221 (44.0)	0.99 (0.76 - 1.30)
2009	257 (48.5)	0.94 (0.73 - 1.23)	241 (45.5)	1.01 (0.78 - 1.31)
<b>Region of residence at death</b>	<i>P</i> < .0001	<i>P</i> < .0001	<i>P</i> < .0001	<i>P</i> < .0001
Calgary	237 (37.7)	ref	206 (32.8)	ref
Edmonton	303 (45.2)	1.36 (1.07 - 1.72)	301 (44.9)	1.60 (1.26 - 2.03)
Northern Alberta	169 (72.8)	5.13 (3.61 - 7.29)	143 (61.6)	3.51 (2.52 - 4.87)
Central Alberta	211 (59.4)	2.75 (2.07 - 3.67)	193 (54.4)	2.65 (2.00 - 3.52)
Southern Alberta	97 (51.6)	1.90 (1.34 - 2.69)	87 (46.3)	1.89 (1.34 - 2.69)
<b>Tumor site</b>	<i>P</i> = .96	<i>P</i> = .41	<i>P</i> = .11	<i>P</i> = .35

Colon	629 (48.9)	ref	554 (43.1)	ref
Rectum	280 (49.0)	0.88 (0.70 - 1.09)	276 (48.3)	1.17 (0.95 - 1.46)
Rectosigmoid	108 (50.0)	0.88 (0.64 - 1.19)	100 (46.3)	1.05 (0.77 - 1.43)
<b>Stage at diagnosis</b>	<b><i>P</i> = .02</b>	<b><i>P</i> = .19</b>	<b><i>P</i> = .10</b>	<b><i>P</i> = .04</b>
IV	148 (50.2)	ref	131 (44.4)	ref
I/II	252 (54.9)	1.26 (0.93 - 1.71)	228 (49.7)	1.30 (0.96 - 1.76)
III	506 (47.1)	1.29 (1.00 - 1.67)	470 (43.7)	1.41 (1.10 - 1.82)
Missing	111 (45.3)	1.11 (0.78 - 1.56)	101 (41.2)	1.27 (0.90 - 1.78)
<b>Duration of disease, months</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> = .25</b>	<b><i>P</i> = .01</b>
1-6	171 (36.3)	ref	199 (42.3)	ref
6-18	325 (53.5)	1.81 (1.37 - 2.40)	312 (51.4)	1.28 (0.98 - 1.69)
18-36	249 (50.6)	1.79 (1.32 - 2.43)	206 (41.9)	0.93 (0.69 - 1.25)
>36	272 (54.0)	1.98 (1.44 - 2.73)	213 (42.3)	0.85 (0.62 - 1.16)
<b>Charlson Comorbidity</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>
0	455 (42.9)	ref	409 (38.5)	ref
1	239 (54.9)	2.01 (1.57 - 2.57)	203 (46.7)	1.51 (1.19 - 1.93)
≥2	323 (55.9)	1.99 (1.59 - 2.50)	318 (55.0)	2.07 (1.66 - 2.59)
<b>Other cancer</b>	<b><i>P</i> = .69</b>	<b><i>P</i> = .04</b>	<b><i>P</i> = .82</b>	<b><i>P</i> = .28</b>
No	759 (48.8)	ref	700 (45.0)	ref
Yes	258 (49.8)	1.27 (1.01 - 1.58)	230 (44.4)	1.13 (0.90 - 1.41)
<b>Consult with oncologist in the last 6 months</b>	<b><i>P</i> = .03</b>	<b><i>P</i> = .03</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> = .003</b>
No	688 (47.5)	ref	601 (41.5)	ref
Yes	329 (52.6)	1.30 (1.02 - 1.65)	329 (52.6)	1.42 (1.12 - 1.79)
<b>Follow-up visit with oncologist in the last 6 months</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .001</b>
No	341 (37.6)	ref	328 (36.2)	ref
Yes	676 (57.9)	1.83 (1.42 - 2.37)	602 (51.6)	1.56 (1.21 - 2.01)

<b>Radiotherapy in the last 6 months</b>	<b><i>P</i> &lt; .0001</b>	<i>P</i> = .29	<b><i>P</i> &lt; .0001</b>	<i>P</i> = .01
No	823 (47.1)	ref	738 (42.2)	ref
Yes	194 (59.7)	1.17 (0.88 - 1.56)	192 (59.1)	1.44 (1.08 - 1.91)
<b>Chemotherapy in the last 6 months</b>	<b><i>P</i> &lt; .0001</b>	<i>P</i> = .43	<b><i>P</i> &lt; .0001</b>	<i>P</i> = .61
No	642 (44.4)	ref	603 (41.7)	ref
Yes	375 (59.7)	1.11 (0.86 - 1.42)	327 (52.1)	1.07 (0.83 - 1.37)

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**Appendix 3.3 Unadjusted and adjusted analysis for having one or more ICU admission in the last 6 months of life**

<b>Characteristics</b>	<b>N (%)</b>	<b>OR (95% CI)</b>
<b>Total</b>	123 (5.9)	—
<b>N of admissions</b>	130	—
<b>Mean[Median] length of stay</b>	21.5 [16]	—
<b>Sex</b>	<i>P</i> = <b>.01</b>	<i>P</i> = <b>.05</b>
Female	41 (4.5)	ref
Male	82 (7.1)	1.50 (0.99 - 2.27)
<b>Age at death, years</b>	<i>P</i> = <b>.24</b>	<i>P</i> = <b>.04</b>
≤60	27 (6.0)	ref
61-70	33 (7.0)	0.98 (0.56 - 1.71)
71-80	39 (6.4)	0.68 (0.38 - 1.21)
>80	24 (4.4)	0.41 (0.21 - 0.82)
<b>Year of death</b>	<i>P</i> = <b>.52</b>	<i>P</i> = <b>.80</b>
2006	31 (6.1)	ref
2007	35 (6.5)	1.00 (0.59 - 1.71)
2008	23 (4.6)	0.78 (0.44 - 1.39)
2009	34 (6.4)	0.99 (0.58 - 1.70)
<b>Region at death</b>	<i>P</i> = <b>.001</b>	<i>P</i> = <b>.02</b>
Calgary	32 (5.1)	ref
Edmonton	27 (4.0)	0.74 (0.43 - 1.29)
Northern Alberta	22 (9.5)	1.68 (0.92 - 3.08)
Central Alberta	22 (6.2)	1.05 (0.58 - 1.90)
Southern Alberta	20 (10.6)	1.97 (1.04 - 3.73)
<b>Tumor site</b>	<i>P</i> = <b>.17</b>	<i>P</i> = <b>.12</b>
Colon	69 (5.4)	ref

Rectum	43 (7.5)	1.57 (1.02 - 2.44)
Rectosigmoid	11 (5.1)	1.12 (0.56 - 2.23)
<b>Stage at diagnosis</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>
IV	47 (4.4)	ref
I/II	27 (9.2)	3.58 (2.00 - 6.41)
III	43 (9.4)	4.25 (2.58 - 6.99)
Missing	6 (2.5)	0.89 (0.35 - 2.28)
<b>Duration of disease, months</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>
1-6	52 (11.0)	ref
6-18	33 (5.4)	0.30 (0.18 - 0.51)
18-36	21 (4.3)	0.19 (0.10 - 0.35)
>36	17 (3.4)	0.12 (0.06 - 0.24)
<b>Charlson Comorbidity Index</b>	<b><i>P</i> &lt; .0001</b>	<b><i>P</i> &lt; .0001</b>
0	38 (3.6)	ref
1	25 (5.7)	1.50 (0.87 - 2.59)
≥2	60 (10.4)	2.70 (1.72 - 4.25)
<b>Other cancer</b>	<b><i>P</i> = .71</b>	<b><i>P</i> = .95</b>
No	94 (6.0)	ref
Yes	29 (5.6)	1.02 (0.64 - 1.62)
<b>Consult with oncologist in the last 6 months</b>	<b><i>P</i> = .53</b>	<b><i>P</i> = .12</b>
No	89 (6.1)	ref
Yes	34 (5.4)	0.68 (0.42 - 1.10)
<b>Follow-up visit with oncologist in the last 6 months</b>	<b><i>P</i> = .24</b>	<b><i>P</i> = .37</b>
No	60 (6.6)	ref
Yes	63 (5.4)	0.78 (0.45 - 1.36)

<b>Radiotherapy in the last 6 months</b>	<i>P</i> = <b>.02</b>	<i>P</i> = .05
No	113 (6.5)	ref
Yes	10 (3.1)	0.48 (0.23 - 1.01)
<b>Chemotherapy in the last 6 months</b>	<i>P</i> = .24	<i>P</i> = <b>.02</b>
No	80 (5.5)	ref
Yes	43 (6.8)	1.91 (1.11 - 3.29)

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**Appendix 3.4 Reasons for having more than one ER visit in the last 30 days of life**

<b>Most responsible diagnoses</b>	<b>Frequency</b>	<b>%</b>
	<b><i>N</i> = 685</b>	
Cancers	152	22.2
Symptoms, signs and abnormal clinical and laboratory findings	147	21.5
Specific procedures and health care, including palliative care, chemotherapy	115	16.8
Diseases of digestive system	81	11.8
Endocrine, nutritional and metabolic diseases	39	5.7
Diseases of respiratory system	31	4.5
Diseases of circulatory system	22	3.2
Injury, complication of surgical or medical care	22	3.2
Diseases of genitourinary system	18	2.6
Infections	14	2.0
Others	44	6.4

**Appendix 3.5 Reasons for having more than one hospitalization in the last 30 days of life**

<b>Most responsible diagnosis</b>	<b>Frequency <i>N</i> = 425</b>	<b>%</b>
Specific procedures and health care, including palliative care, chemotherapy	163	38.4
Cancers	99	23.3
Diseases of digestive system	53	12.5
Symptoms, signs and abnormal clinical and laboratory findings	29	6.8
Diseases of circulatory system	17	4.0
Infections	12	2.8
Diseases of respiratory system	10	2.4
Injury, complication of surgical or medical care	10	2.3
Endocrine, nutritional and metabolic diseases	8	1.9
Diseases of genitourinary system	8	1.9
Others	16	3.8

**Appendix 3.6 Reasons for ICU admission in last 30 days of life**

<b>Most responsible diagnosis</b>	<b>Frequency <i>N</i> = 47</b>	<b>%</b>
Cancers	16	34.1
Gastrointestinal diseases	9	19.2
Infections	5	10.6
Diseases of respiratory system	5	10.7
Diseases of circulatory system	4	8.5
Palliative care	3	6.4
Others	5	10.6

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## Chapter 4 General Discussion and Conclusions

### 4.1 Summary

#### 4.1.1 Summary of the First Paper (Chapter 2)

During the year 2002-2005 in Alberta, about 50% of patients with surgically treated stage III colon or stage II/III rectal adenocarcinoma did not receive guideline-recommended adjuvant chemotherapy. Following previous studies that investigated patient factors that influenced the receipt of adjuvant chemotherapy,<sup>1,2</sup> this study assessed the association between oncologists and patient's not receiving adjuvant chemotherapy.

Our results showed that among patients who had an oncologist-consult (80% of all surgically treated patients), 26.4%, 40.9%, and 25.6% of patients with stage III colon, stage II rectal, and stage III rectal adenocarcinoma, respectively, did not receive adjuvant chemotherapy. Across the three cancer types, the oncologist-specific odds of patients' receiving versus not receiving chemotherapy varied significantly, after adjusting for case-mix (i.e., sex, age and co-morbidity). Variation by oncologist was largest for stage II rectal cancer and smallest for stage III colon cancer. The number of oncologists who had highly elevated odds of patients' not receiving chemotherapy compared with the Alberta average was greater for stage II rectal cancer than for stage III rectal and colon cancer.

The variation by oncologist was possibly related to some patient factors that were unavailable to us but potentially influence treatment choice, e.g., patient preference, functional status, or

contraindication to chemotherapy. But it is unlikely, however, that a given oncologist would have higher percentage of patients with these or similar issues than other oncologists. Therefore, it is unlikely that other factors would explain the variation we observed in treatment pattern by oncologist. Alternatively, the variation could be explained by a lack of consensus among oncologists with respect to adjuvant chemotherapy for certain types of patients, despite guideline recommendation.

The wider variation among oncologists for rectal cancer, especially stage II rectal cancer, is concerning because it implies that delivery of guideline-recommended adjuvant chemotherapy highly depends on oncologist. The discrepancy across the cancer types/stages may be related to the differences in management strategies for colon and rectal cancers, despite some similarities between them. For stage III colon cancer, adjuvant chemotherapy following surgery has been the only standard treatment over the past 20 years: the positive survival effect of adjuvant chemotherapy has been conclusively established.<sup>3</sup> By contrast, treatment guidelines for stage II/III rectal cancer are more complex and are subject to new findings.<sup>4-6</sup> There is growing evidence in support of neoadjuvant treatment over the last decades.<sup>7-9</sup> The most recent practice guidelines updated by the Gastrointestinal Cancer Disease Site Group in Ontario recommend preoperative chemoradiation over a postoperative approach based on the available evidence when both options are feasible.<sup>6</sup> During the time period for our study, however, preoperative therapy was relatively new and uncommon. It is, therefore, unlikely that use of preoperative chemoradiation affected the decision to use adjuvant chemotherapy. In fact, only a small percentage of patients received preoperative radiation or chemotherapy during this time period.<sup>2</sup>

To date, adjuvant chemotherapy remains a component of standard treatment for stage II/III rectal cancer in Canada.<sup>6</sup>

Our study indicates potential inconsistency among oncologists in administering guideline-based adjuvant chemotherapy for patients with stage III colon or stage II/III rectal cancer in Alberta. It suggests oncologists impact the variation in the receipt of standard treatment. Given the large percentage of patients not receiving treatment according to guidelines and the inconsistency among physicians in referring and treating, our findings emphasize the need to develop strategies aimed at improving consensus amongst treating physicians and suggest a need to implement ongoing monitoring of referral and treatment patterns.

Based on findings from this study and our previous studies, we have initiated knowledge exchange activities among relevant stakeholders. Through a series of meetings, our findings were disseminated to communities of surgeons and oncologists to heighten their awareness of the low rates of guideline-consistent practice in the province and the variation in referral and treatment patterns. At the provincial Gastrointestinal Tumor Group meeting, oncologists received their own results with respect to numbers and percentages of patients that they treated as well as the overall provincial average. This information allowed them to assess their treatment patterns relative to their peers. Further knowledge translation efforts are under development.

#### *4.1.2 Summary of the Second Paper (Chapter 3)*

In the second study, we examined service utilization and evaluated the aggressiveness of EOL cancer care for CRC patients in Alberta. Based on a cohort of patients who died of CRC in years 2006-2009, five indicators for poor quality of EOL cancer care were measured: receiving chemotherapy in the last 14 days of life, having more than one ER visit, more than one hospitalization, or at least one ICU admission in the last 30 days of life, and dying in an acute-care hospital. Due to data limitations, we did not examine another important aspect of EOL care, namely, the receipt of palliative care.

Our results showed that of 2,074 patients included, 55% had at least one indicator of poor quality EOL care. The most prevalent was death in an acute care hospital, which occurred for half of the patients. The other events had much lower frequency: during the last 30 days of life, one in eight had multiple ER visits, one in ten had multiple hospitalizations, and 2% had an ICU admission. Less than 4% of patients received chemotherapy in the last two weeks of life. Demographic and clinical characteristics were associated with the EOL care quality indicators including sex, age, region of residence, cancer stage, duration of disease and comorbidity. Calendar year, sub-site of CRC, and history of other cancer were not associated with the measurement of indicators.

Regional variation in the quality indicators of EOL care was striking. Patients who resided in rural regions had higher uses of almost all of the acute hospital care services measured than those

in urban regions. Patients in Calgary were least likely and patients in Northern Alberta were most likely to have multiple ER visits, hospitalizations and die in an acute care hospital. Compared with patients in Calgary, patients in Northern Alberta had over 4 times the odds of having more than one ER visit, 5 times odds of having more than one hospitalization in the last 30 days of life, and close to 8 times odds of dying in acute care hospital, after adjusting for relevant characteristics. The regional disparity is potentially due to the uneven allocation of health resources and development of palliative care in rural regions. Edmonton and Calgary were among the first palliative care champions in Canada; innovative palliative care programs were introduced in the mid-1990s. By the year 2000, comprehensive palliative care programs had been fully developed in the two metropolitan areas.<sup>10</sup> By contrast, rural regions are relatively short of care resources such as palliative facilities and providers. The urban/rural disparity suggests the need to increase these services in rural regions.

In this study, we also found that having an oncologist-consult at the end of life was positively associated with aggressive use of hospital outpatient and inpatient care; this is intriguing. Given that cancer specialists have more experience in caring for terminally ill patients and the palliative care teams that exist within the urban cancer facilities, it is expected that a patient who has an oncologist visit should have a developed and well-functioning plan for the EOL care. Further investigation is needed to understand the reasons for this association.

This study is the first study in Alberta measuring quality indicators for EOL care. It established a methodology template in Alberta that links various data sources for EOL care study. It has underscored the need for additional research. Using CRC as the starting point, the methodology could extend to EOL care evaluation for other cancers. Population-based quality indicators allow us to compare care across the institutions or regions and over time, thereby helping identify potential opportunities for system improvement and promote better health care policies for the dying. Continuous measurement of these indicators can provide useful information for health planners and administrators, aiding for decision making and system improvement. Using administrative data is efficient for quality care surveillance, which can complement other methods for EOL care research, such as qualitative and prospectively-collected clinical data.<sup>11</sup>

Findings of this study will be disseminated to relevant stakeholders. As a first step, informal meetings will be held with health professionals, including cancer care providers and program managers, to discuss the findings from this study and obtain their perspectives about the findings and related issues they have identified. Intervention studies, additional analyses and further research may be generated from such discussions in order to improve understanding and address identified issues. Knowledge dissemination will also be made to health administrators, program planners, and policy makers to initiate discussions towards implementation of ongoing measurement for EOL care and assess the need for targeted changes to address disparities found.

## 4.2 Recommendations and Suggested Future Research

- In order to improve receipt of standard cancer care, efforts are needed to improve consensus amongst physicians on the value of adjuvant chemotherapy. Clinical leadership is needed for this to occur.
- The rate of consultation and the rate of use of treatment consistent with guideline should be monitored to evaluate the success of any interventions and/or to assess whether change occurs in the absence of formal intervention.
- Further evidence on the value of adjuvant chemotherapy is needed for developing clearer treatment guidelines, particularly for rectal cancer<sup>12</sup>, which can be achieved by more direct and definitive evidence from randomized control trials and population-level observational studies.
- An improved linked data system that includes palliative care services at the provincial level is needed to complement the current data sources and enable further population-based research on EOL care.
- To allow effective comparison across jurisdictions nationwide, standardized definitions and methods for EOL care evaluation is suggested.
- Conduct intervention studies to improve and evaluate guideline-consistent cancer care and EOL care in Alberta for CRC patients.

### **4.3 Conclusion**

Given the relatively high proportion of CRC patients who did not receive guideline-consistent adjuvant chemotherapy and the variation among oncologists in treating pattern, improvement at the system level is needed to ensure the optimal care for CRC patients.

The study reported the utilization of chemotherapy and acute care for colorectal cancer patients close to the end of life. The large regional variation in EOL care quality suggests the need to enhance the quality of EOL care and ensure accessibility to high-quality care for the dying, especially in rural areas of Alberta.

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