Waiting Time Intervals for Non-Small Cell Lung Cancer Diagnosis and Treatment in Alberta: Quantification of Intervals and Identification of Risk Factors Associated with Delays

By

Julian Oliver Anthony Kim

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Department of Public Health Sciences

University of Alberta

Abstract

Background: Very little is known regarding the time required to diagnose and treat patients with Non-Small Cell Lung Cancer (NSCLC) in Canada. Prompt diagnosis and treatment is critical for optimizing the quality and effectiveness of NSCLC care.

Purpose: To quantify the duration of diagnostic and treatment intervals for NSCLC care in Alberta and identify risk factors associated with delayed diagnosis and treatment.

Methods: The Alberta Cancer Registry was used to identify all cases of pathologically confirmed, stage I to III NSCLC diagnosed and treated in Alberta, Canada from 2004 to 2011. Diagnostic data were obtained from provincial physician billing and inpatient/outpatient hospital data. Missing data were obtained manually from electronic medical records. Data from all sources were linked to quantify the duration of the diagnostic and treatment intervals and their sum (system interval). Multivariable logistic regression was performed in order to identify which patient, disease, and treatment factors were independently associated with diagnostic or treatment delays.

Results: 3009 eligible patients were included in the study; the median and 90th percentile system interval was 78 (95% CI 76-80) and 185 days (95% CI 178 to 195), respectively. Overall, the treatment interval was longer than the diagnostic interval, with median of 51 (95% CI 49-53) and 38 (95% CI 36-40) days, respectively. After multivariable adjustment, age above 60, and treatment with modalities other than supportive care, especially surgery (OR for treatment delay = 5.23, $p<0.0001$) were associated with delays. Factors associated with prompt care included

high acuity presentations (OR for delayed diagnosis = 0.34, $p<0.0001$), and stage III disease (OR for delayed treatment = 0.38, $p<0.0001$).

Conclusion: Over 50% of Albertans with potentially curable NSCLC experienced considerably long diagnostic and/or treatment intervals. Factors influencing the probability of delay in decreasing order of importance were: first treatment modality, acuity level of presentation, stage, and age. The results of this study suggest that care intervals could be shortened for NSCLC patients through the use of streamlined coordination of care, especially for those who require surgery.

Preface

This thesis is an original work by Julian O.A. Kim. The research project, of which this thesis is a part, received research ethics board approval from The Human Research Ethics Board of the University of Alberta, project name “Population based evaluation of quality and timeliness of lung cancer care”, ID number: Pro0031009, 22 June 2012.

Dedication

I dedicate my dissertation work to my wife, Christina, and my children Alyssa and Isabelle. Without their tenacious love and support, the completion of this thesis would have not been possible. I would also like to dedicate this work to my parents, Dr. Bong-Hwan & Mrs. Hong Ja Kim who have always demonstrated the value of lifelong learning in their own lives which has served to inspire me to do likewise. Finally, I would like to dedicate this thesis to Mr. Michael and Dr. Joan Lim whose support to my family during the completion of this Master of Science degree was indispensable and greatly appreciated.

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Table of Contents

List of Tables

List of Figures

List of Abbreviations

ACR = Alberta Cancer Registry
AHS = Alberta Health Services
AJCC = American Joint Committee On Cancer
ATOP = Alberta Thoracic Oncology Program
BTS = British Thoracic Society
CT = Computed Tomography
CXR = Chest X-Ray
DBI = Diagnostic Biopsy Interval
DI = Diagnostic Interval
DII = Diagnostic Imaging Interval
EMR = Electronic Medical Record
ICBP = International Cancer Benchmarking Partnership
MRI = Magnetic Resonance Imaging
OR = Odds Ratio
PET = Positron Emission Tomography
SI = System Interval
SES = Socioeconomic Status
TI = Treatment Interval
NSCLC = Non-Small Cell Lung Cancer

Chapter 1: Introduction

Lung cancer is the number one cause of cancer mortality for men and women worldwide (1). Non-small cell lung cancer (NSCLC) is the most common form of lung cancer, accounting for approximately 85% of incident cases in Canada (2), where an estimated 26,100 incident cases of lung cancer will be diagnosed in 2014, of whom 20,500 will die from their disease (3). Non-Small Cell Lung Cancer constitutes approximately 85% (2) of all incident cases of lung cancer. The majority these cases are diagnosed at either locally advanced (27.4%) or metastatic (47.9%) stages (2) largely owing to the lack of population level screening for NSCLC as well as the relatively hasty growth kinetics inherent to NSCLC (4). Non-Small Cell Lung Cancer is associated with poor survival with an overall 5 year survival rate of only 15.9% (5) with 5 year survivals of 45-49%, 30-31%, 5-14% and 1% for AJCC stage I, II, III, and IV disease respectively.

NSCLC Diagnostic Pathway

The diagnosis of NSCLC is a complex and time consuming process involving interactions between numerous healthcare providers and organizations (Figure 2.1). In general, patients with potentially curable NSCLC typically present to their family physician, specialist, or local emergency room with symptomatic concerns such as cough, shortness of breath, fatigue, or weight loss. A diagnostic workup typically ensues which includes a diagnostic imaging scan (Chest X-Ray and/or CT-scan of the Chest and upper abdomen).

Should any of these scans demonstrate a lesion suspicious for malignancy, a referral is made to a specialist (respirologist, thoracic surgeon, or interventional radiologist) in order to obtain a biopsy for pathological confirmation of the imaging findings by any of the following means: bronchoscopy, mediastinoscopy, sputum cytology, image guided lung biopsy, image guided lymph node/solid organ biopsy, thoracoscopic biopsy, or thoracentesis. The biopsy specimens are sent for pathological evaluation and oftentimes, repeat biopsies are required (due to non-diagnostic biopsy samples which can arise as a result of sampling errors at the time of the procedure) in order to achieve the final tissue diagnosis.

After pathological confirmation of the biopsy specimen as NSCLC a patient is referred to a specialist (medical oncologist, radiation oncologist, thoracic surgeon, or palliative care specialist) for consideration of treatment. Under the supervision of a specialist, a staging workup is conducted in order to establish the clinical stage of the disease as well as to assess if a patient is fit to undergo treatment. The staging workup generally includes combinations of any of the following: pulmonary function testing, electrocardiogram, positron emission tomography (PET) scan, bone scan, and imaging of the brain (either a computed tomography (CT) or magnetic resonance imaging (MRI) scan). Alternatively, should imaging scans show early stage NSCLC without evidence of metastasis, a thoracic surgeon may opt to resect the primary tumour with a lobectomy or a wedge-resection without prior pathological confirmation since both of these procedures are considered to be simultaneously diagnostic and curative for early stage, PET positive, lung nodules. Treatment commences as soon as a consented patient has completed all of the staging workup and the necessary resources required for treatment (such as the operating room or linear accelerator used for radiotherapy) become available for the patient.

NSCLC Care

Depending on the stage of the NSCLC, the patient's level of comorbidities, ability to undergo surgical interventions, as well as the patient's preferences, treatment options for stage I to III NSCLC could include any combinations of the following:

1) Surgical Resection (generally radical intent); or
2) Radiation Therapy (either radical or palliative intent); or
3) Chemotherapy (either radical or palliative intent); or
4) Best Supportive Care (palliative intent care measures which do not involve chemotherapy, radiotherapy, or surgical management).

Waiting Time Intervals for NSCLC Diagnosis and Care

Waiting times experienced by NSCLC patients are the product of the disequilibrium between the health care system's supply of diagnostic and treatment services and the demand for these services arising from the population, inefficiencies in coordination and communication between health care professionals, lack of defined diagnostic practice standards, and an absence of system performance auditing mechanisms. The Romanow Report (6) established that the health care system in Canada suffers from widespread protracted waiting times for diagnostic procedures as well as a lack of accurate data regarding waiting times for them. Several reports (7, 8) have established that there are widespread protracted diagnostic and treatment intervals for cancer patients in Canada. Very little is known with respect to the benchmark durations of the diagnosis and treatment intervals of patient with NSCLC in Canada.

The growth, division, and metastatic progression of NSCLC is an inexorable process with tumour potential doubling times reported as swift as 11 days (9). Excessive delays in the diagnosis and treatment of NSCLC have been associated with increased tumour bulk, worsening of respiratory symptoms, and the progression of disease from potentially curable to incurable disease (10). Protracted diagnostic and treatment delays are also associated with intensification of the psychological distress (11) experienced by cancer patients, deflating the morale of both patients and caregivers as well as detracting from the perceived quality of care of lung cancer patients. As well, jurisdictions, namely Denmark, which have reduced care interval delays for NSCLC patients have demonstrated significant improvements in overall survival at the population level (12). For these reasons, the minimization of diagnostic and treatment intervals for NSCLC care is imperative.

Research efforts into the timeliness of care of NSCLC patients in the past decade within Canada has been limited to small retrospective chart review based cohort studies of either surgical (13), adjuvant chemotherapy (14), or radiotherapy (15) waiting times. To date, no Canadian groups have published large, population based, assessments of diagnostic or treatment intervals for NSCLC patients.

A recent study conducted by the International Cancer Benchmarking Partnership (ICBP) compared survival outcomes from twelve different jurisdictions in six different developed nations from 1995 to 2007 (16). This study demonstrated significant disparities in survival between Canadian jurisdictions whereby lung cancer patients in Alberta had the shortest 1 & 5 year age-adjusted survival when compared to lung cancer patients from other Canadian

jurisdictions (British Columbia, Ontario, and Manitoba). Since survival is an indicator of the overall effectiveness of health services, the results of the ICBP study suggest a potential for improvement in the survival of lung cancer patients in Alberta should systematic improvements in diagnostic and treatment services be carried out.

International Guidelines for the Timeliness of Lung Cancer Diagnosis and Treatment

Recognizing that the diagnostic pathway for NSCLC is a time consuming journey, several working groups have published recommendations regarding the optimal duration of the diagnostic work-up for NSCLC. The British Thoracic Society (BTS) was the first group to produce recommended waiting times (17) for lung cancer diagnosis and treatment. These guidelines were largely based on clinical opinion due to the lack of conclusive evidence supporting their suggested timelines of care. In 1998, the BTS recommended that the maximum waiting time for assessment by a respiratory specialist of 1 week if a patient had clinical evidence of lung cancer. Furthermore, the total delay from referral for imaging scans to initial consultation with a respiratory specialist was to be no longer than 2 weeks. Finally, the total duration between a request for biopsy and the tissue diagnosis to be communicated with the patient was to be no longer than 2 weeks. In 2003, the American College of Chest Physicians adopted the BTS recommendations (18) and incorporated their timetable of care for NSCLC into their guidelines. Other countries, such as Denmark, have made use of legislation in order to drive the timeliness of care for NSCLC patients. By act of parliament, the maximal interval from specialist referral to treatment (treatment interval) is to be 42 days or less for 85% of all Danish NSCLC patients (12).

Alberta Initiatives to Improve Lung Cancer Diagnostic and Treatment Intervals

In light of the potential for improved survival identified by the ICBP study, Alberta Health Services (AHS) announced their intention to prioritize the rapid diagnosis and treatment of patients with Lung Cancer. In December 2011, AHS announced the creation of a $15.4M program, the Alberta Thoracic Oncology Program (ATOP), that established rapid access clinics in Edmonton & Calgary with the aim of shortening the diagnostic wait times for 75% of Lung Cancer patients from the onset of symptoms to treatment decision to ≤30 days and waiting time from referral to surgery of ≤60 days (19). Through the ATOP funding, AHS aims to increase the number of diagnostic bronchoscopies performed per year by 70% and increase the number of CT-guided biopsies by 46%.

While the goals set by AHS for ATOP seem ambitious, other groups have successfully shortened diagnostic waiting times for NSCLC though the use of nursing navigators (20), telemedicine multidisciplinary meetings (21), and reorganization of services within a cancer network (22). Although it is expected that the AHS ATOP initiative should shorten the diagnostic intervals for NSCLC patients, due diligence is required to assess the effectiveness of the ATOP initiative and the impact of this intervention on patient centered outcomes.

Study Aims

This thesis will serve to quantify the time intervals that patients with NSCLC in Alberta with potentially curable disease (stage I to III) spend waiting for their diagnosis (diagnostic interval),

treatment (treatment interval) and their sum (system interval). Furthermore, this thesis will seek to determine which patient, disease, and treatment factors are independently associated with delayed diagnostic, treatment, and system intervals.

References

1. Cancer fact sheet [homepage on the Internet]. Geneva, Switzerland: World Health Organization. 2014 February 2014. Available from: http://www.who.int/mediacentre/factsheets/fs297/en/.

2. Canadian Partnership Against Cancer. Lung cancer in canada: A supplemental system performance report. Toronto: Canadian Partnership Against Cancer; 2010.

3. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian cancer statistics 2014. Toronto, Ontario: Canadian Cancer Society; 2014.

4. Friberg S, Mattson S. On the growth rates of human malignant tumors: Implications for medical decision making. J Surg Oncol. 1997 Aug;65(4):284-97.

5. Howlader N, Noone A, Krapcho M, Neyman N, Aminou R, Altekruse S, et al. SEER cancer statistics review, 1975-2009 (vintage 2009 populations). Bethesda, MD: National Cancer Institute; 2011.

6. Romanow R. Builiding on values: The future of health care in canada. Ottawa, Ontario: Commission on the Future of Health Care in Canada; 2002.

7. Wait Time Alliance. Time for transformation: Canadians still waiting too long for health care. Ottawa (ON): Wait Time Alliance for Timely Access to Health Care; 2013.

8. Wait Time Alliance. Its about time! achieving benchmarks and best practices in wait time management. Ottawa (Ontario): Wait Time Alliance for Timely Access To Health Care; 2005.

9. Wilson GD, McNally NJ, Dische S, Saunders MI, Des Rochers C, Lewis AA, et al. Measurement of cell kinetics in human tumours in vivo using bromodeoxyuridine incorporation and flow cytometry. Br J Cancer. 1988 Oct;58(4):423-31.

10. O'Rourke N, Edwards R. Lung cancer treatment waiting times and tumour growth. Clin Oncol (R Coll Radiol). 2000;12(3):141-4.

11. Risberg T, Sorbye SW, Norum J, Wist EA. Diagnostic delay causes more psychological distress in female than in male cancer patients. Anticancer Res. 1996 Mar-Apr;16(2):995-9.

12. Jakobsen E, Green A, Oesterlind K, Rasmussen TR, Iachina M, Palshof T. Nationwide quality improvement in lung cancer care: The role of the danish lung cancer group and registry. J Thorac Oncol. 2013 Oct;8(10):1238-47.

13. Liberman M, Liberman D, Sampalis JS, Mulder DS. Delays to surgery in non-small-cell lung cancer. Can J Surg. 2006 Feb;49(1):31-6.

14. Saint-Jacques N, Rayson D, Al-Fayea T, Virik K, Morzycki W, Younis T. Waiting times in early-stage non-small cell lung cancer (NSCLC). J Thorac Oncol. 2008 Aug;3(8):865-70.

15. Johnston GM, MacGarvie VL, Elliott D, Dewar RA, MacIntyre MM, Nolan MC. Radiotherapy wait times for patients with a diagnosis of invasive cancer, 1992-2000. Clin Invest Med. 2004 Jun;27(3):142-56.

16. Coleman MP, Forman D, Bryant H, Butler J, Rachet B, Maringe C, et al. Cancer survival in australia, canada, denmark, norway, sweden, and the UK, 1995-2007 (the international cancer benchmarking partnership): An analysis of population-based cancer registry data. Lancet. 2011 Jan 8;377(9760):127-38.

17. BTS recommendations to respiratory physicians for organising the care of patients with lung cancer. the lung cancer working party of the british thoracic society standards of care committee. Thorax. 1998 Jun;53 Suppl 1:S1-8.

18. Alberts WM, Bepler G, Hazelton T, Ruckdeschel JC, Williams JH,Jr, American College of Chest Physicians. Lung cancer. practice organization. Chest. 2003 Jan;123(1 Suppl):332S-7S.

19. Alberta Health Services. Program to deliver faster treatment for lung cancer patients. News Release. Calgary, Alberta: Alberta Health Services; 2011 16 December 2011.

20. Hunnibell LS, Rose MG, Connery DM, Grens CE, Hampel JM, Rosa M, et al. Using nurse navigation to improve timeliness of lung cancer care at a veterans hospital. Clin J Oncol Nurs. 2012 Feb;16(1):29-36.

21. Davison AG, Eraut CD, Haque AS, Doffman S, Tanqueray A, Trask CW, et al. Telemedicine for multidisciplinary lung cancer meetings. J Telemed Telecare. 2004;10(3):140-3.

22. Leary A, Corrigan P. Redesign of thoracic surgical services within a cancer network-using an oncology focus to inform change. Eur J Oncol Nurs. 2005 Mar;9(1):74-8.

Chapter 2: Quantification of the Diagnostic and Treatment Intervals for Patients with Stage I to III Non-Small Cell Lung Cancer in Alberta, Canada

Introduction

Lung cancer is the leading cause of cancer mortality for both men and women in Canada (1). In 2014, it is estimated that some 26,100 new cases of lung cancer will be diagnosed in Canada of who 20,500 will die of their disease (1). Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all incident cases of lung cancer in Canada (2) and is associated with a poor overall 5 year survival rate of only 15.9% (3).

The diagnosis and treatment of lung cancer is clinically complex and requires patients to interact with different facets of the health care system. System delays experienced by patients are the product of the disequilibrium of the health care system's supply of diagnostic and treatment services and the demand for these services which arise from the population (4), inefficiencies in coordination and communication between involved health care professionals, lack of defined diagnostic practice standards, and absence of system performance auditing mechanisms. Several reports (5, 6) have established that there are widespread protracted diagnostic and treatment intervals for cancer patients in Canada and, furthermore, that there is a lack of accurate data regarding the duration of these delays (4). Very little, however, is known regarding how long it takes to diagnose and treat NSCLC in Canada.

The growth of lung cancer is an inexorable process with tumour potential doubling times as swift as 11 days (7). Excessive delays in the diagnosis and treatment of NSCLC have been associated with increased tumour bulk, worsening of respiratory symptoms, and the progression of disease from potentially curable to incurable disease (8). Protracted diagnostic and treatment delays are also associated with intensification of the psychological distress (9) experienced by cancer patients, deflating the morale of both patients and caregivers as well as detracting from the quality of care of lung cancer patients. As well, jurisdictions, namely Denmark, which have reduced care interval delays for NSCLC patients have demonstrated significant improvements in overall survival at the population level (10). For these reasons, the minimization of diagnostic and treatment intervals for NSCLC care is imperative.

A recent study conducted by the International Cancer Benchmarking Partnership (ICBP) compared survival outcomes from twelve different jurisdictions in developed nations from 1995 to 2007. This study demonstrated significant disparities in survival whereby lung cancer patients in the province of Alberta had the shortest 1 & 5 year age-adjusted survival amongst the Canadian jurisdictions included in the study (11). Since survival is an indicator of the overall effectiveness of health services, the results of the ICBP study suggest that there is potential for improvement in the survival of lung cancer patients in Alberta should systematic improvements in diagnostic and treatment services be carried out.

We present a quantitative analysis of time to diagnosis and treatment, and interval components thereof, experienced by patients with stage I to III NSCLC diagnosed and treated in Alberta from 2004 to 2011 as a means to identify inequalities and opportunities for improvement in the quality and effectiveness of care for patients with NSCLC.

Methods

Study Population & Data Sources

Alberta Health Services is the sole provider of oncology services for the publicly insured population of Alberta, Canada (a population of approximately four million persons). The Alberta Cancer Registry (ACR) served as the primary data source for patient, pathological, and treatment variables for the study cohort. The ACR was queried to identify all adults with histologically confirmed, incident cases of potentially curable (stage I to III) NSCLC diagnosed from 2004 to 2011 using the following International Classification of Diseases for Oncology (IDC-O) codes: 8070/3 (Squamous Cell Carcinoma), 8140/3 (Adenocarcinoma), 8012/3 (Large Cell Carcinoma), 8046/3 (Non-Small Cell Carcinoma). For each patient identified, the following variables were extracted from the ACR: region of residence and age at diagnosis, gender, marital status, diagnosis date, TNM stage at diagnosis (AJCC 6th ed.), date of first oncologist consultation, first treatment modality, and date of first treatment. The year 2004 was chosen as the start date of the study period as electronic medical records were routinely available for manual abstraction of missing data for all patients diagnosed after 1 January 2004.

This data was linked to provincially administered health care databases using the unique provincial health identification number of each NSCLC case. Diagnostic imaging and biopsy procedure data were obtained from physician billing and inpatient/outpatient hospital administrative databases including: dates of chest x-rays (CXR) within 1 year of, CT scans within 6 months of diagnosis, and biopsy procedures performed within 6 months of tissue diagnosis (bronchoscopy, CT or ultrasound guided biopsies, mediastinoscopy, sputum cytology, thorascopic biopsies, thoracentesis, and lymph node biopsies), and presence or absence of comorbid conditions which could have potentially hastened the diagnostic process (pneumonia, or pulmonary embolism). Patients were deemed to have had a high acuity presentation for purposes of this analysis if they satisfied any of the following criteria: 1) Inpatient hospital admission for 96 hours or longer within 30 days of their diagnosis; 2) pulmonary embolism or pneumonia within 30 days of diagnosis. Outpatient billing records and inpatient/outpatient hospital diagnostic codes were utilized to capture all comorbid conditions diagnosed or treated within 1 year of each patient's date of NSCLC diagnosis. The Charlson Comorbidity score (12, 13) was then calculated using all identified comorbid conditions for each patient in order to quantify levels of comorbidity for individual patients.

Patient demographic variables pertaining to socioeconomic status were obtained at the aggregate level using federal government census data including: median household income, and education level (prevalence of high school diploma) for the postal code of each patient's residence at the time of diagnosis.

In the event that data were missing from the linked administrative databases pertaining to the date and time of diagnostic imaging scans, biopsies, or treatment, the Cancer Control Alberta electronic medical record (EMR) and/or paper chart was manually queried and consultation notes, diagnostic imaging and pathology reports were reviewed in order manually impute missing data.

Patients were excluded from the study if they were either diagnosed or had their treatment performed outside of the province of Alberta, had prior malignancies within 5 years prior to NSCLC diagnosis (with exception of non-melanoma skin cancers), or if EMR/paper records were unavailable for imputation of missing data.

Care Path Interval Definitions

The Refined Anderson Model of Total Patient Delay (14) and Arhus Consensus Statement (15) on the reporting of diagnostic and treatment pathways for cancer diagnosis were utilized to select milestones to define the beginning and end of each interval. Ideally, the total waiting interval experienced by patients should begin on the day that their symptoms began (14, 15); however, given the administrative nature of our linked databases, it was impossible to reliably capture this milestone. As well, since lung cancer patients typically have other chronic medical conditions (such as chronic obstructive pulmonary disease, hypertension, or coronary artery disease) which require frequent visits to a primary care provider, the identification of the first primary care provider milestone visit which triggered the first diagnostic procedure also proved to be infeasible given the administrative nature of our data. As such a proxy date (the date of initial chest x-ray) was chosen by necessity to define the beginning of the diagnostic

interval (See Table 2.1 and Figure 2.1 for definitions of each time interval). The Diagnostic Interval (DI) was broken down into two stepwise interim intervals: 1) The Diagnostic Imaging Interval (DII); and 2) The Diagnostic Biopsy Interval (DBI). The DII was defined as the time elapsed between the date of last chest-x-ray which immediately preceded the last CT scan prior to the first diagnostic biopsy attempt to the date of the last CT scan prior to the first diagnostic biopsy attempt. The DBI was defined as the interval elapsed between the date of the last CT scan prior to the first diagnostic biopsy attempt to the date of the diagnostic biopsy procedure which provided the pathological diagnosis (the diagnosis date). The DI was defined as the interval from the beginning of the DII to the end of the DBI. The Treatment Interval (TI) was defined as the period of time elapsed from the diagnosis date to the first day of treatment. The System Interval (SI) was defined as the time elapsed from the beginning of the DII to the end of the TI.

Analysis

The distribution of patient characteristics, disease, and treatment factors were calculated overall and by modality of the first treatment. Differences in distributions were compared using the chi-squared or anova tests. The median, 25^{th}, 75^{th} and 90^{th} percentiles and corresponding 95 percent confidence intervals were calculated for each interval (SI, DI, DII, DBI, and TI) and cumulative distribution function curves were generated for each time interval stratified by first treatment received. The log-rank test was used to assess for statistically significant differences between treatment modalities for each cumulative distribution function curve.

The Alberta Thoracic Oncology Program (ATOP) was launched at the end of the study period (December 2011) with the aim of streamlining the care of lung cancer patients via improved coordination of patient care and increased availability of bronchoscopic and CT-guided biopsy procedures (16). ATOP set benchmark goals for diagnostic and treatment intervals for lung cancer patients as follows: 1) Interval from symptom onset to treatment decision of ≤30 days; and 2) interval from referral to surgery of ≤60 days for 75 percent of all patients. For exploratory purposes, the proportion of patients who conformed to the ATOP interval benchmark goals were quantified for our study cohort. For these comparisons, the diagnostic interval was used as a proxy for the first ATOP benchmark interval, and the treatment interval for those who received surgery was used as a surrogate to second ATOP interval (from referral to surgery).

Ethical Considerations

This study was conducted with the approval of the Human Research Ethics Board of the University of Alberta (Edmonton, Alberta, Canada).

Results

From 2004 to 2011, there were 3100 incident cases of, biopsy confirmed, stage I to III NSCLC diagnosed in Alberta. Of these, 647 cases had one or more missing biopsy or diagnostic imaging date from the linked administrative databases and were subject to manual audits.

Of the 3100 cases, 91 were excluded from the study for the following reasons: 1) no EMR or paper chart data available upon manual audit (n=43); 2) diagnosis or treatment

performed outside of Alberta (n=16); 3) prior malignancy (n=13); 4) stage IV disease (n=12); 5) incorrect pathology (n=2); 6) duplicate record (n=1); and 7) diagnosis outside of the study dates (n=1).

Table 2.2 describes the distribution of patient and disease characteristics overall and by modality of the first treatment. The median age of patients was 69 (range 38-95) and stage distribution was: stage I (28.9%); stage 2 (8.9%); stage 3 (62.2%). Radiotherapy (42.6%) was the most common first treatment modality followed by surgery (30%), supportive care (19.2%), and chemotherapy (10.2%). Adenocarcinoma (41.2%) and squamous cell carcinoma (34.7%) were the most common pathological subtypes amongst the cohort. The majority of patients lived in either the Edmonton (35.3%) or Calgary (30.5%) geographic zones at the time of their diagnosis. A slight predominance of male patients was observed (54% versus 46%). Most of the cohort (64.3%) had at least one significant medical comorbidity (Charlson Score ≥ 1), and patients managed with supportive care were observed to have the highest proportion of patients with ≥ 2 medical comorbidities (44.4%, $P<0.0001$) when compared to patients treated with another modality of care.

High acuity presentations for care were observed in 30.3% of the overall cohort. By stage, high acuity presentations were more frequent amongst those with stage III disease (36%) when compared with stage I or II disease (21%), ($p<0.0001$)

System Interval

The median and 90th percentile of the overall system interval was 78 (95% CI 76 -80) and 185 (95% CI 178-195) days, respectively (Table 2.3). The system interval varied markedly by treatment modality such that the median SI for patients whose first treatment was surgery was 105 days (95% CI 102-110), 44% longer ($p<0.0001$) than either radiotherapy or chemotherapy (Figure 2.2). This is due, in part, to heterogeneity of patient characteristics between treatment groups at diagnosis such as a low proportion of high acuity presentations amongst surgical patients (14.4%) as compared to those treated with chemotherapy (31.3%), radiotherapy (31.3%), or supportive care (49.6%) ($p<0.0001$). The length of the system interval was also strongly associated with stage, whereby those with stage III disease had markedly shorter system intervals (64 days; 95% CI 62 -67) than those with stage I (102 days; 95% CI 98 - 108) or II disease (103 days; 95% CI 96-112) ($p<0.0001$).

Diagnostic Imaging Interval

Almost all patients (99.6%) had at least one diagnostic imaging test performed prior to their first biopsy. Of the 2998 patients who underwent diagnostic imaging, 1944 (64.6%) had both CXR and CT imaging, 898 (29.8%) had CT imaging only, while 156 (5.2%) had CXR imaging only prior to their first attempt at a diagnostic biopsy.

The median and 90th percentile diagnostic imaging interval was 10 (95% CI 9-11) and 71 (95% CI 63-82) days, respectively (Table 3). As such, the DII comprised the shortest

interim interval of both the diagnostic interval and system interval for the entire cohort. Patients whose first treatment was surgery had the longest DII ($p<0.0001$) with median and 90th percentile durations of 14 (95% CI 13-16) and 85 (95% CI 71-106) days, respectively (Table 2.3 and Figure 2.3).

Diagnostic Biopsy Interval

The vast majority of the cohort (97.5%) had at least one attempt at obtaining a pathological diagnosis prior to treatment with 62.9% of the cohort having at least one operative biopsy (bronchoscopy, mediastinoscopy, or pleural biopsy), and 74.1% having at least one non-operative attempt at a pathological diagnosis (sputum cytology, thoracentesis, Image guided biopsy, or lymph node biopsy). Of those who did not have a pathological diagnosis prior to treatment, the majority (73 of 76) were treated surgically with a wedge resection or lobectomy, which are both considered to be diagnostic and therapeutic for small pulmonary nodules that are highly suspicious for malignancy based on preoperative CT or positron emission tomography (PET) scans. Patients requiring both operative and non-operative biopsies had a longer median DBI (22 days; 95% CI 20.2 to 23.8) when compared to those requiring either non-operative (12 days; 95% CI 9.8 to 14.2) or operative biopsies only (19 days; 95% CI) ($p<0.0001$).

The median and 90th percentile DBI for the entire cohort was 19 (95%CI 17-20) and 91 (95% CI 84-98) days respectively (Table 2.3, Figure 2.4). Patients treated surgically experienced the longest median DBI of 27 days (95% CI 23-29) ($p<0.0001$) while those treated with supportive care had the shortest median biopsy waiting time of 15 days (95%

CI 13-18). Patients who required 2 or ≥3 biopsy attempts waited, on average, an additional 7.5 and 34.9 days longer ($p<0.0001$) than those who only required one biopsy in order to make a diagnosis. Of note, the proportion of patients requiring more than one attempt at biopsy was the smallest amongst those treated with surgery (47.9%) when compared to either radiotherapy (54.2%) or chemotherapy (51.9%) ($p = 0.008$).

Treatment Interval

Regardless of modality of the first treatment, the largest component of the system interval was the treatment interval. Overall, the median and 90th percentile treatment interval was 51 (95% CI 49-53) and 124 (95% CI 118-129) days, respectively (Table 2.3, Figure 2.5). Those whose first treatment was surgery had the longest treatment intervals with a median TI of 73 days (95% CI 70-77). By contrast, patients receiving either radiotherapy or chemotherapy had significantly shorter median treatment intervals of 49 days ($P<0.0001$).

Proportion Conforming to ATOP Benchmarks

A minority of the cohort (42.7%) conformed to the first ATOP benchmark goal (Interval from symptom onset to treatment decision of 30 days) using the DI as a proxy for comparison to the benchmark. Amongst those who conformed to this ATOP benchmark, a large portion (43.2%) had high acuity presentations, and locally advanced disease (62.2%). Patients managed by best supportive care had the highest proportion (50%) that

conformed to the first ATOP Benchmark while those whose first treatment was surgery had the lowest (32%) ($p<0.0001$).

For those treated surgically, 38.6% conformed to the second ATOP benchmark goal (interval from referral to surgery of 60 days) using the TI as a proxy for comparison to the benchmark.

Discussion

The primary aim of this study was to quantify the absolute durations of the system interval and its component interim intervals experienced by Albertans with stage I to III NSCLC. Furthermore, we sought to identify which component of their care paths comprised the greatest portion, or tightest bottleneck, of the system interval. To this end, we have established that overall, Albertans tend to wait considerably long for both the diagnosis and treatment of their potentially curable disease and that the greatest proportion of the system interval is the treatment interval. As such, any initiative aimed at reducing the system interval for Albertans with NSCLC should incorporate a strategy to minimize treatment intervals, especially for those who require surgery.

There are a number of potential explanations for the protracted intervals experienced by surgical patients in our cohort. Firstly, surgical patients require more comprehensive cardiopulmonary assessments prior to their treatment date when compared to non-surgically treated NSCLC patients. These assessments could include any combination of the following examinations: Electrocardiograms, echocardiograms, lung

ventilation/perfusion scans, pulmonary function testing, anesthesia consultations, and PET scans. Navigating patients through these additional assessments undoubtedly consumes considerable time and demands a greater amount of coordination by the ordering physician. Enhancing the coordination of these pre-treatment medical assessment through use of nursing navigators (17), multidisciplinary meetings (18), streamlining of services within a cancer network (19), and implementation of referral guidelines (20) have all been shown to reduce system delays for cancer patients and thus represent logical measures to evaluate and/or implement in Alberta's case. Secondly, a paradoxical disparity was apparent in our analysis whereby patients with the least probability of cure (those with locally advanced disease) had the swiftest journeys through the system, meanwhile, those with the best chance of a cure (patients with stage I or II disease who are most likely to require surgery) waited almost 60% percent longer. This phenomenon, known as the "waiting time paradox" (21), has been observed in other cancer disease sites that lack effective screening measures which, in turn, skews the stage distribution towards locally advanced presentation with high acuity symptoms that necessitate inpatient admission and investigation. Until screening for NSCLC is implemented at the population level, a system wide initiative to emphasize expedited care for patients with earlier stage disease is warranted to ensure that the rapid triage of those with high stage disease with high acuity symptoms does not jeopardize opportunities for cure amongst those with earlier stage disease.

The major strength of this study is its large, population-based, sample size of NSCLC patients (n=3009) which were identified by the Alberta Cancer Registry. The Alberta

Cancer Registry is evaluated annually by the North American Association of Comprehensive Cancer Registries and has consistently achieved its highest level of certification (22). As such, our study's population represents essentially all biopsy confirmed, NSCLC cases (stage I to III) diagnosed and treated in Alberta during the study dates; the findings are therefore widely generalizable. Furthermore, since the study period represented a contemporary era (2004-2011), the patterns of practice and care paths which were examined in this study are largely identical to those in clinical use today and electronic medical records were available to retrieve missing administrative data.

The limitations of this study primarily stem from its population-based design. Given the administrative nature of the primary data sources, the milestones used to define intervals were proxy dates by necessity which resulted in intervals which were less patient-centric and more administrative in quality. Furthermore, the use of a proxy date for the milestone which marked the beginning of the DI (the last chest-x-ray prior to the first CT scan which immediately proceeded the first attempt at diagnostic biopsy) almost certainly underestimated the true duration of both the diagnostic and system intervals since the use of this proxy excluded the time interval from a patient's first presentation to their primary care provider to the date of their initial chest x-ray. As well, we were unable to quantify certain socioeconomic variables at the individual level (most notably income and education level) and instead relied upon aggregate level census data. This may have had the effect of masking potential trends between certain socioeconomic strata and the urgency in which diagnostic evaluations were pursued. Finally, data regarding the timing

and frequency of PET scans were not available for this analysis due to the presence of alternative remuneration plans for nuclear imaging specialists in Alberta. Since PET scans were employed routinely during most of the study period, differences in patterns of practice in the scheduling and frequency of PET scans between treatment modalities may have differentially prolonged time intervals for certain subsets of patients, especially for those who were treated radically. Given the limitations of our data, we were not able to assess for this effect.

Numerous groups have published benchmarks goals for the various intervals and delays associated with lung cancer care as a means to stimulate quality improvement. In 1998, the BTS recommended a maximum interval for assessment by a respiratory specialist of 1 week if a patient had clinical evidence of lung cancer. Furthermore, the total interval from referral for imaging scans to initial consultation with a respiratory specialist was to be no longer than 2 weeks (23). In 2003, the American College of Chest Physicians adopted the BTS recommendations (24) and incorporated their timetable of care for NSCLC into their guidelines. In Denmark, by act of legislation, the maximal interval from specialist referral to treatment (treatment interval) is to be no longer 42 days for 85% of all patients (10). By the end of the study period, largely as a result of the prolonged intervals discussed in this study, the Alberta Thoracic Oncology Program (ATOP) was created in order to attempt to streamline care for NSCLC patients. ATOP set bold benchmark goals for lung cancer patients of ≤30 days from onset of symptoms to treatment decision and a ≤60 days from referral to surgery for 75% of all patients. Our analysis has shown that from 2004 to 2011, our healthcare system was well behind both

ATOP and international benchmarks for NSCLC diagnosis and treatment. Furthermore, our analysis suggests that the attainment of both of the ATOP benchmarks would be virtually unobtainable without incurring stifling costs to the healthcare system given that many of those who conformed to the benchmarks required inpatient admission in order to do so. As such, the ATOP benchmarks goals should be further assessed in light of the findings of this study.

Conclusion

Albertans with Stage I to III NSCLC experienced considerably long intervals for their diagnosis and treatment during the study period. Due to the use of proxy dates, the estimates of the diagnostic and system intervals for our cohort are almost certainly underestimations of the true durations of the care intervals experienced by our patients. The largest component of the system interval for all NSCLC care was found to be the treatment interval. Interval inequities were apparent whereby patients who were treated surgically experienced the longest system and interim intervals. The results of this study justify the need to streamline the care paths of NSCLC patients, particularly for those who are managed surgically.

References

1. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian cancer statistics 2014. Toronto, Ontario: Canadian Cancer Society; 2014.

2. Canadian Partnership Against Cancer. Lung cancer in canada: A supplemental system performance report. Toronto: Canadian Partnership Against Cancer; 2010.

3. Howlader N, Noone A, Krapcho M, Neyman N, Aminou R, Altekruse S, et al. SEER cancer statistics review, 1975-2009 (vintage 2009 populations). Bethesda, MD: National Cancer Institute; 2011.

4. Romanow R. Builiding on values: The future of health care in canada. Ottawa, Ontario: Commission on the Future of Health Care in Canada; 2002.

5. Wait Time Alliance. Time for transformation: Canadians still waiting too long for health care. Ottawa (ON): Wait Time Alliance for Timely Access to Health Care; 2013.

6. Wait Time Alliance. Its about time! achieving benchmarks and best practices in wait time management. Ottawa (Ontario): Wait Time Alliance for Timely Access To Health Care; 2005.

7. Wilson GD, McNally NJ, Dische S, Saunders MI, Des Rochers C, Lewis AA, et al. Measurement of cell kinetics in human tumours in vivo using bromodeoxyuridine incorporation and flow cytometry. Br J Cancer. 1988 Oct;58(4):423-31.

8. O'Rourke N, Edwards R. Lung cancer treatment waiting times and tumour growth. Clin Oncol (R Coll Radiol). 2000;12(3):141-4.

9. Risberg T, Sorbye SW, Norum J, Wist EA. Diagnostic delay causes more psychological distress in female than in male cancer patients. Anticancer Res. 1996 Mar-Apr;16(2):995-9.

10. Jakobsen E, Green A, Oesterlind K, Rasmussen TR, Iachina M, Palshof T. Nationwide quality improvement in lung cancer care: The role of the danish lung cancer group and registry. J Thorac Oncol. 2013 Oct;8(10):1238-47.

11. Coleman MP, Forman D, Bryant H, Butler J, Rachet B, Maringe C, et al. Cancer survival in australia, canada, denmark, norway, sweden, and the UK, 1995-2007 (the international cancer benchmarking partnership): An analysis of population-based cancer registry data. Lancet. 2011 Jan 8;377(9760):127-38.

12. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis. 1987;40(5):373-83.

13. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the charlson comorbidity index predicted in-hospital mortality. J Clin Epidemiol. 2004 Dec;57(12):1288-94.

14. Walter F, Webster A, Scott S, Emery J. The andersen model of total patient delay: A systematic review of its application in cancer diagnosis. J Health Serv Res Policy. 2012 Apr;17(2):110-8.

15. Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S, et al. The aarhus statement: Improving design and reporting of studies on early cancer diagnosis. Br J Cancer. 2012 Mar 27;106(7):1262-7.

16. Alberta Health Services. Program to deliver faster treatment for lung cancer patients. News Release. Calgary, Alberta: Alberta Health Services; 2011 16 December 2011.

17. Hunnibell LS, Rose MG, Connery DM, Grens CE, Hampel JM, Rosa M, et al. Using nurse navigation to improve timeliness of lung cancer care at a veterans hospital. Clin J Oncol Nurs. 2012 Feb;16(1):29-36.

18. Davison AG, Eraut CD, Haque AS, Doffman S, Tanqueray A, Trask CW, et al. Telemedicine for multidisciplinary lung cancer meetings. J Telemed Telecare. 2004;10(3):140-3.

19. Leary A, Corrigan P. Redesign of thoracic surgical services within a cancer network-using an oncology focus to inform change. Eur J Oncol Nurs. 2005 Mar;9(1):74-8.

20. Neal RD, Din NU, Hamilton W, Ukoumunne OC, Carter B, Stapley S, et al. Comparison of cancer diagnostic intervals before and after implementation of NICE guidelines: Analysis of data from the UK general practice research database. Br J Cancer. 2014 Feb 4;110(3):584-92.

21. Crawford SC, Davis JA, Siddiqui NA, de Caestecker L, Gillis CR, Hole D, et al. The waiting time paradox: Population based retrospective study of treatment delay and survival of women with endometrial cancer in scotland. BMJ. 2002 Jul 27;325(7357):196.

22. Tucker TC, Howe HL, Weir HK. Certification for population-based cancer registries. J Reg Mgmt. 1999;26:24-27.

23. BTS recommendations to respiratory physicians for organising the care of patients with lung cancer. the lung cancer working party of the british thoracic society standards of care committee. Thorax. 1998 Jun;53 Suppl 1:S1-8.

24. Alberts WM, Bepler G, Hazelton T, Ruckdeschel JC, Williams JH,Jr, American College of Chest Physicians. Lung cancer. practice organization. Chest. 2003 Jan;123(1 Suppl):332S-7S.

Table 2.1: Definitions of Diagnostic, Treatment and System Intervals

Time Interval	Start of Interval	End of Interval
Diagnostic Imaging Interval (DII)	Date of the CXR which immediately preceded the last CT Scan prior to the first diagnostic biopsy attempt*	Date of the last CT Scan Prior to the first diagnostic biopsy attempt
Diagnostic Biopsy Interval (DBI)	Date of the last CT Scan Prior to the first attempt at diagnostic biopsy	Date of the diagnostic biopsy procedure which provided the pathological diagnosis
Diagnostic Interval (DI)	Beginning of DII	End of DBI
Treatment Interval (TI)	Date of diagnostic biopsy procedure which provided the pathological diagnosis	First day of treatment[#]
System Interval (SI)	Beginning of DII	End of TI

[*]Note: For patients whose disease was first detected on CT imaging without any preceding CXR imaging, the diagnostic imaging waiting time was defined as the period between the second last and the last CT scan prior to the first diagnostic biopsy attempt. For patients without CT imaging prior to biopsy, the time interval between the second last and last CXR prior to the first diagnostic biopsy attempt was used as the diagnostic imaging waiting time.

[#] if a given patient did not receive oncologic treatment for their NSCLC, the date of their first oncologist consultation was used in lieu of the first day of treatment for calculation of either the treatment waiting time or the overall waiting time.

Table 2.2: Patient Characteristics at Diagnosis Overall and by Modality of First Treatment

		First Treatment Modality				
	Overall (n=3009)	**Radiotherapy (n= 1281)**	**Surgery (n = 842)**	**Chemotherapy (N= 307)**	**Supportive Care (N= 579)**	**P – value**
Age (median, range)	69 (38 - 95)	70 (38 - 95)	66 (39 -87)	65 (38-89)	75 (42 -95)	<0.0001
Gender						0.001
Female	1383 (46%)	542 (42.3%)	427 (50.7%)	139 (45.3%)	275 (47.5%)	
Male	1626 (54%)	739 (57.7%)	415 (49.3%)	168 (54.7%)	304 (52.5%)	
Stage (AJCC 6th ed)						<0.0001
I	869 (28.9%)	188 (14.7%)	539 (64.0%)	4 (1.3%)	138 (23.8%)	
II	268 (8.9%)	73 (5.7%)	158 (18.8%)	15 (4.9%)	23 (3.8%)	
III	1872 (62.2%)	1020 (79.6%)	145 (17.2%)	288 (93.8%)	419 (72.4%)	
NSCLC type						<0.0001
Adenocarcinoma	1239 (41.2%)	371 (29.0%)	487 (57.8%)	157 (51.1%)	224 (38.7%)	
Squamous Cell	1045 (34.7%)	545 (42.5%)	250 (29.7%)	67 (21.8%)	183 (31.6%)	
NSCLC NOS	615 (20.4%)	328 (25.6%)	49 (5.8%)	75 (24.4%)	163 (28.2%)	
Large Cell	110 (3.7%)	37 (2.9%)	56 (6.7%)	8 (2.6%)	9 (1.6%)	
Year of Diagnosis						<0.0001
2004-2005	650 (21.6%)	333 (26.0%)	149 (17.7%)	63 (20.5%)	105 (18.1%)	
2006-2007	770 (25.6%)	350 (27.3%)	204 (24.2%)	82 (26.7%)	134 (23.1%)	
2008-2009	772 (25.7%)	294 (23.0%)	240 (28.5%)	90 (29.3%)	148 (25.6%)	
2010-2011	817 (27.2%)	304 (23.7%)	249 (29.6%)	72 (23.5%)	192 (33.2%)	
Geographic Zone						<0.0001
Edmonton	1062 (35.3%)	408 (31.9%)	325 (38.6%)	121 (39.4%)	208 (35.9%)	
Calgary	919 (30.5%)	477 (37.2%)	230 (27.3%)	68 (22.1%)	144 (24.9%)	
Central	433 (14.4%)	170 (13.3%)	120 (14.3%)	40 (13.0%)	103 (17.8%)	
North	326 (10.8%)	112 (8.7%)	110 (13.1%)	47 (15.3%)	57 (9.8%)	
South	269 (8.9%)	114 (8.9%)	57 (6.8%)	31 (10.1%)	67 (11.6%)	
High Acuity Presentation						
No	2079 (69.7%)	872 (68.1%)	721 (85.6%)	211 (69.7%)	292 (50.4%)	<0.0001
Yes	912 (30.3%)	408 (31.9%)	121 (14.4%)	96 (31.3%)	287 (49.6%)	
Lives Alone						<0.0001
No	1661 (55.2%)	736 (57.5%)	454 (54%)	201 (65.7%)	270 (46.4%)	

Yes	1156 (38.4%)	539 (42.1%)	221 (26.2%)	104(33.9%)	292 (50.4%)	
Unknown	192 (6.4%)	6 (0.5%)	166 (19.7%)	1 (0.3%)	19 (3.3%)	
Charlson Score						<0.0001
0	1,076 (35.8%)	454 (35.4%)	363 (43.1%)	126 (41.0%)	133 (23.0%)	
1	1,176 (39.1%)	529 (41.3%)	326 (38.7%)	132 (43.0%)	189 (32.6%)	
≥2	757 (25.2%)	298 (23.3%)	153 (18.2%)	49 (16%)	257 (44.4%)	
Median Household Income ($CAD)	56,400	56,400	58,800	59,100	51,200	<0.0001
Education Level*						0.005
1st quartile	744 (25.0%)	307 (24.3%)	196 (23.4%)	70 (23.0%)	171 (30.0%)	
2nd quartile	738 (24.8%)	300 (23.7%)	225 (26.9%)	68 (22.3%)	145 (25.4%)	
3rd quartile	751 (25.2%)	350 (27.7%)	187 (22.3%)	80 (26.2%)	134 (23.5%)	
4th quartile	746 (25.0%)	309 (24.4%)	229 (27.4%)	87 (28.5%)	121 (21.2%)	

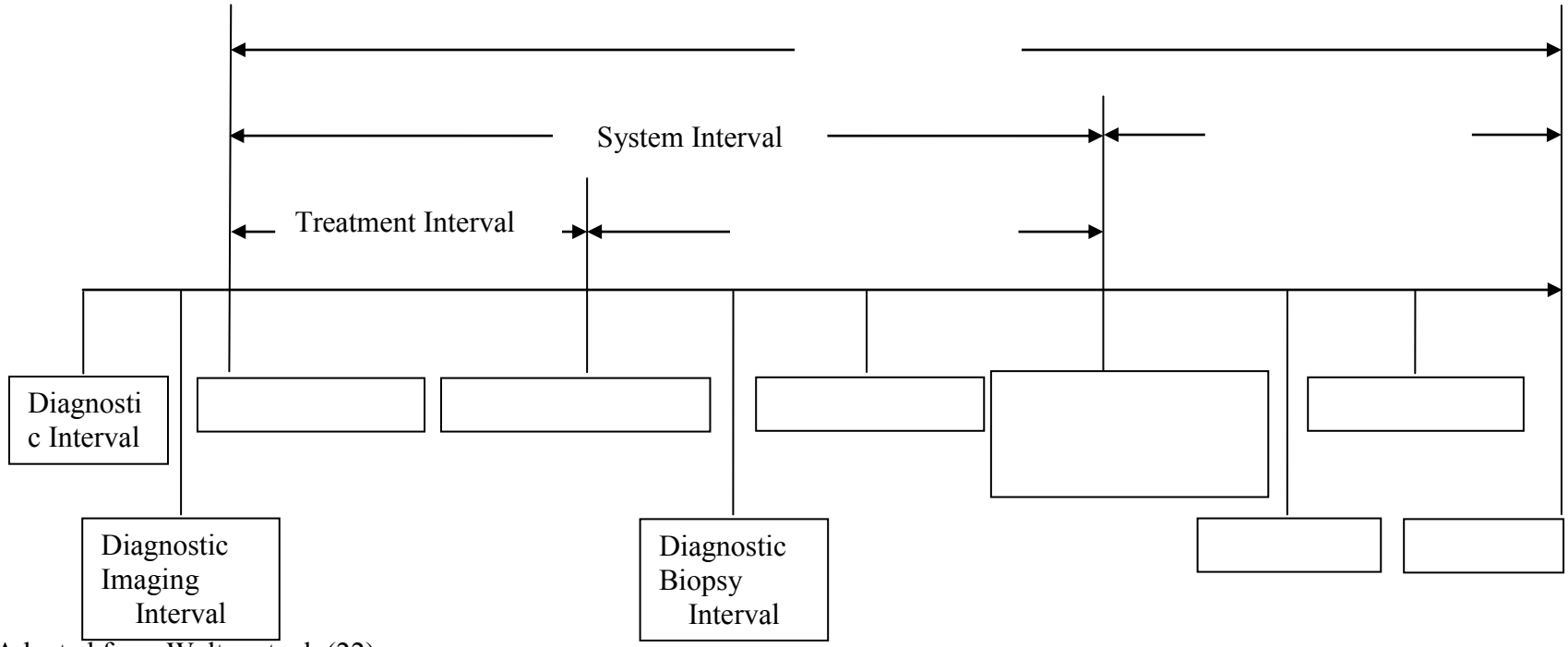
***Prevalence of high school diploma or higher.**

Table 2.3 – Length of Diagnostic, Treatment, and System Intervals by Treatment Modality

	System Interval (Days) with 95% CI			
Treatment Modality	**25th percentile**	**50th percentile**	**75th percentile**	**90th Percentile**
Entire Cohort	46 (43-48)	78 (76-80)	123 (119–126)	185 (178-195)
Radiotherapy	47 (44-49)	73 (70-77)	114 (110-120)	174 (161-183)
Surgery	77 (72-80)	105 (102-110)	147 (140-157)	210 (198-224)
Supportive Care	20 (16-23)	41 (36-45)	83 (73-100)	182 (147-218)
Chemotherapy	50 (44-55)	73 (69-79)	110 (100-120)	167 (144-184)
	Diagnostic Imaging Interval (Days) with 95% CI			
Treatment Modality	**25th percentile**	**50th percentile**	**75th percentile**	**90th Percentile**
Entire Cohort	0 (0-0)	10 (9-11)	28 (26-30)	71 (63-82)
Radiotherapy	0 (0-0)	11 (9-13)	28 (25-32)	67 (56-78)
Surgery	0 (0-0)	14 (13-16)	34 (29-37)	85 (71-106)
Supportive Care	0 (0-0)	3 (2-6)	23 (20-30)	83 (58-107)
Chemotherapy	0 (0-0)	7 (4-10)	22 (20-26)	49 (38-65)
Diagnostic Biopsy Interval (Days) with 95% CI				
	25th percentile	**50th percentile**	**75th percentile**	**90th Percentile**
Entire Cohort	6 (5-6)	19 (17-20)	43 (40-45)	91 (84-98)
Radiotherapy	6 (5-7)	17 (15-19)	36 (34-38)	71 (63-80)
Surgery	7 (5-10)	27 (23-29)	60 (55-64)	105 (98-116)
Supportive Care	4 (3-5)	15(13-18)	40 (33-50)	122 (99-145)
Chemotherapy	6 (3-7)	16 (12-19)	37 (31-43)	74 (55-88)
Diagnostic Interval (Days) with 95% CI				
Entire Cohort	16 (15-17)	38 (36-40)	78 (74-82)	148 (140-161)
Radiotherapy	15 (13-17)	35 (33-37)	71 (64-77)	136 (121-155)
Surgery	24 (21-27)	49 (46-53)	91 (83-101)	155 (142-178)
Supportive Care	11 (9-13)	30 (25-35)	79 (68-101)	200 (170-242)
Chemotherapy	12 (9-15)	33 (26-38)	63 (55-76)	114 (97-134)

Treatment Interval (Days) with 95% CI				
	25th percentile	**50th percentile**	**75th percentile**	**90th Percentile**
Entire Cohort	30 (29-32)	51 (49-53)	82 (79-85)	124 (118-129)
Radiotherapy	30 (29-32)	49 (47-50)	73 (69-76)	112 (106-121)
Surgery	46 (42-49)	73 (70-77)	106 (102-111)	146 (134-156)
Supportive Care	21 (20-22)	31 (28-34)	47 (41-56)	84 (70-118)
Chemotherapy	32 (29-35)	49 (44-52)	73 (64-81)	115 (98-125)

Figure 2.1 – Diagnostic, Treatment, and System Intervals



Adapted from Walter et. al. (22)

Figure 2.2 – System Interval by Treatment Modality

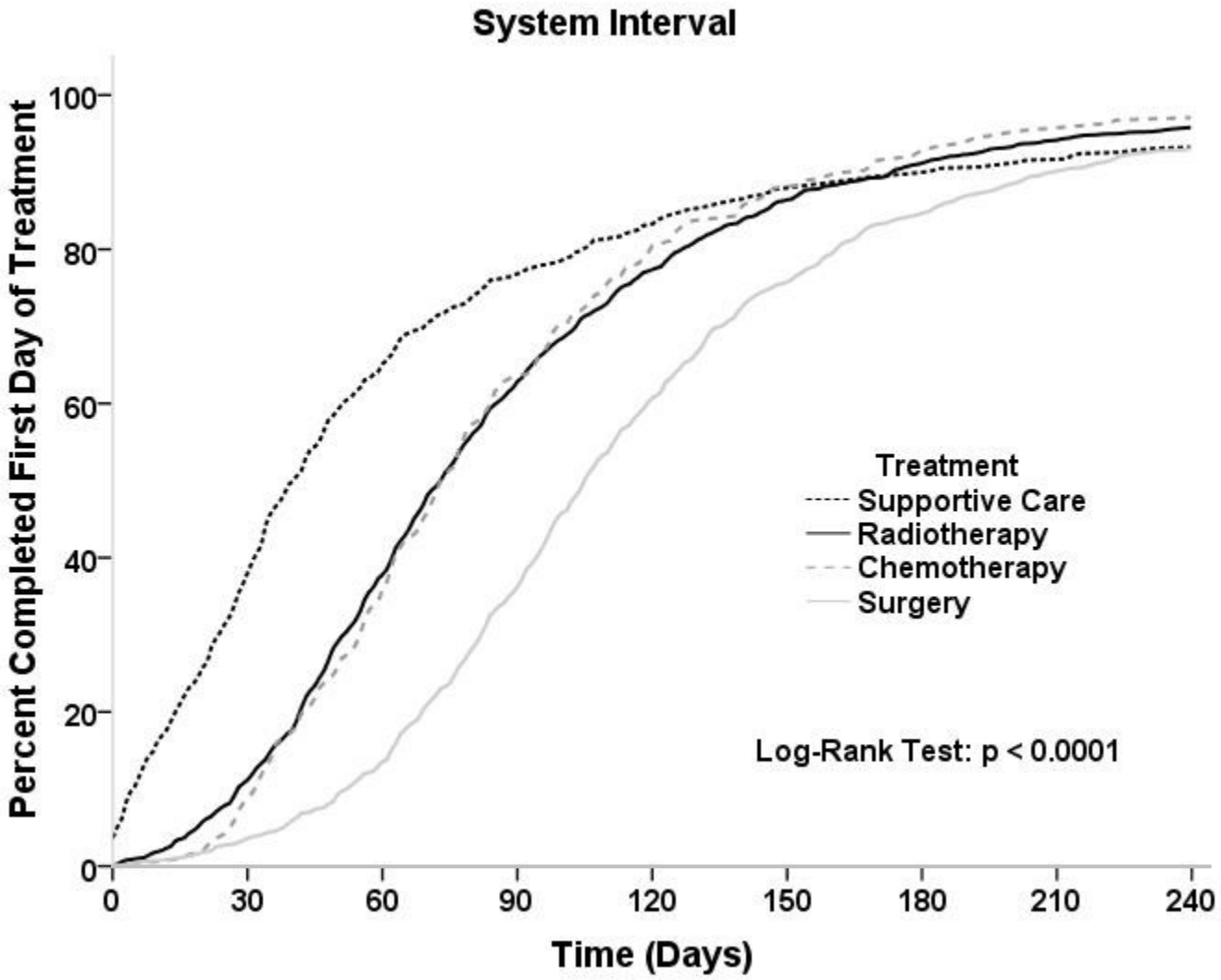


Figure 2.3 – Diagnostic Imaging Interval by Treatment Modality

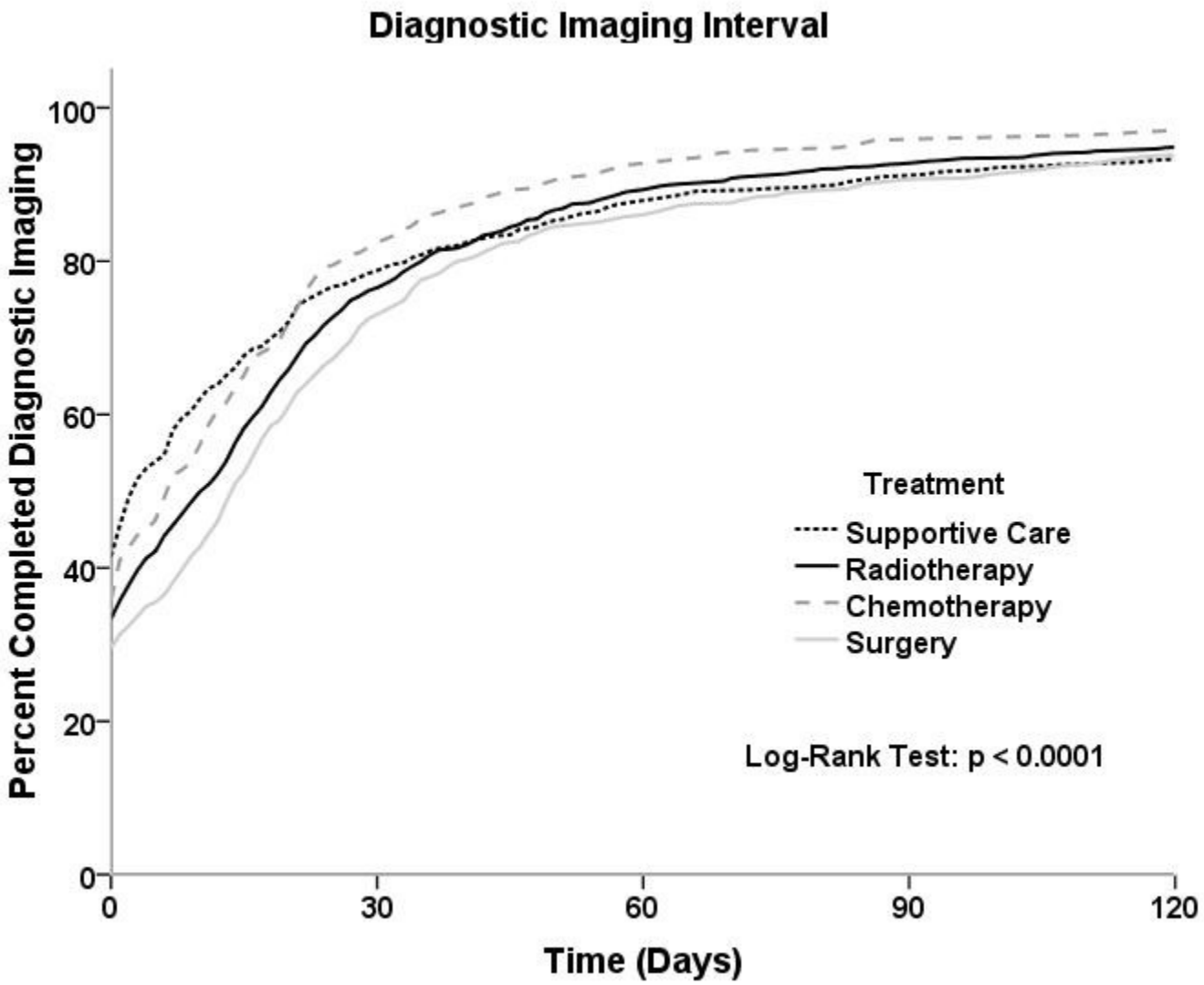


Figure 2.4 - Diagnostic Biopsy Interval by Treatment Modality

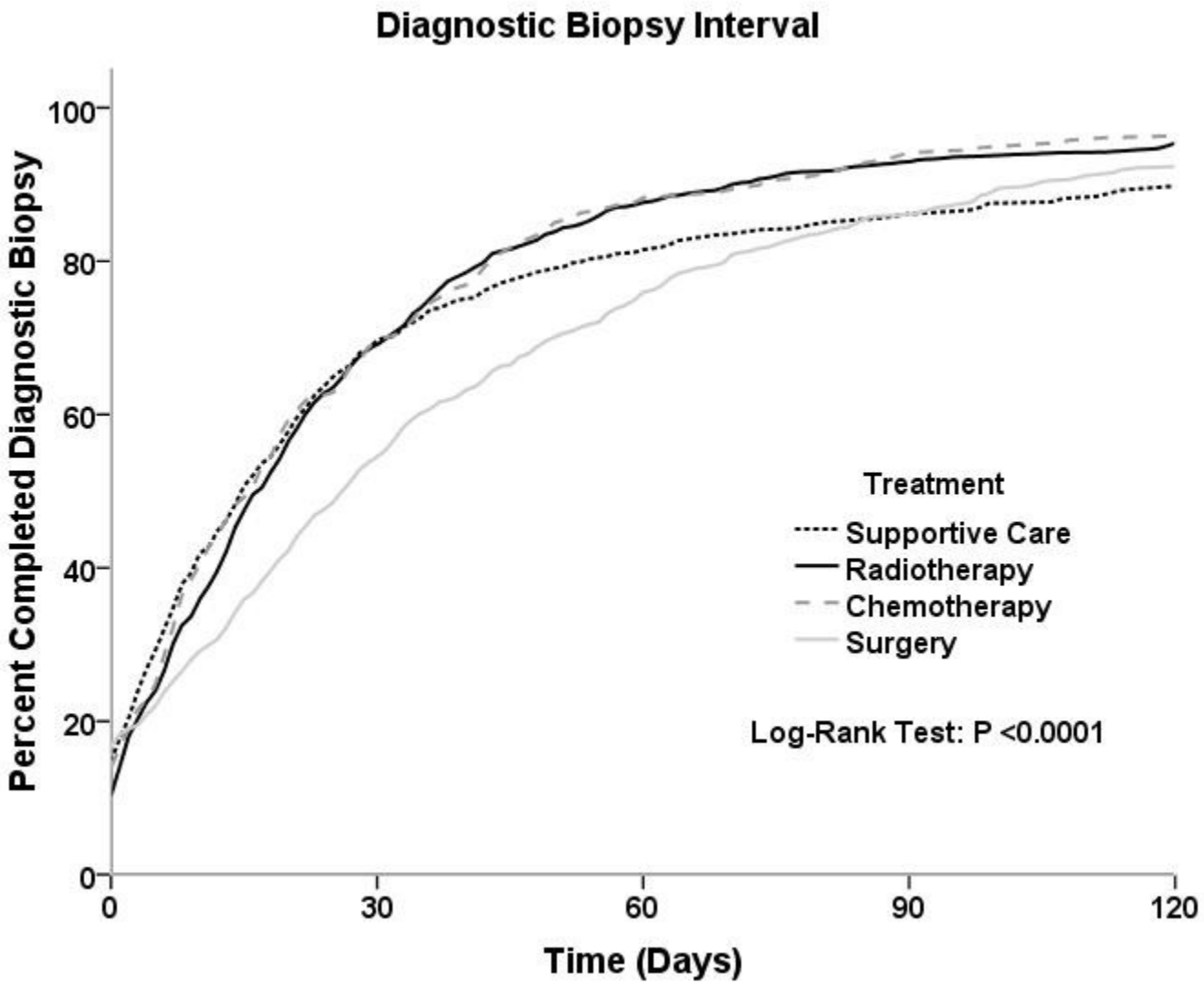
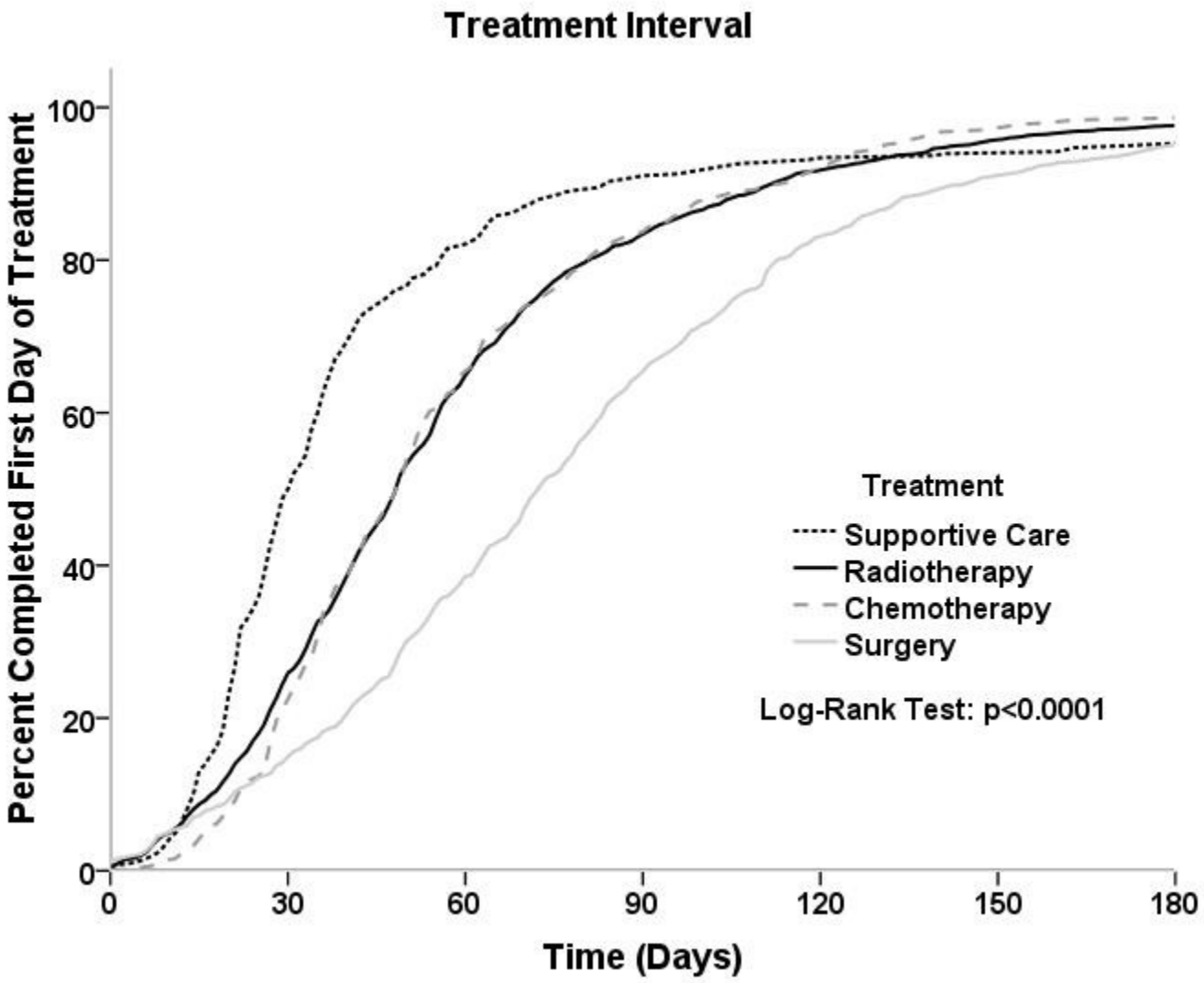


Figure 2.5 - Treatment Interval by Treatment Modality



Chapter 3: Influence of patient, disease, and treatment factors on the time intervals to diagnosis and treatment for patients with stage I to III non-small cell lung cancer in Alberta, Canada

Introduction

Lung cancer is the number one cause of cancer mortality for men and women worldwide (1). Non-small cell lung cancer (NSCLC) is the most common form of lung cancer, accounting for approximately 85% of incident cases in Canada (2), where an estimated 26,100 incident cases of lung cancer will be diagnosed in 2014, of whom 20,500 will die from their disease (3). The high mortality rates of NSCLC are due, in large part, to the high proportion of cases that present with either locally advanced or metastatic disease, for which the chance of cure is minimal (2).

The diagnosis and treatment of NSCLC requires a complex array of imaging and biopsy procedures, interdisciplinary consultations, and pre-treatment assessments. This process is time consuming and can result in delays for some patients. Delays in diagnosis and treatment of cancer have been associated with increased patient and family distress (4), progression of tumours to inoperable disease (5), and inferior treatment outcomes (6-8). Reduction in delays in the NSCLC care paths have resulted in improved overall survival in some jurisdictions, namely Denmark (9). A recent assessment of the timeliness of NSCLC diagnosis and treatment (Chapter 2) in Alberta, Canada (a publicly funded and administered healthcare system) has determined that a majority of patients experienced diagnostic and treatment delays that were well in excess of local and international guidelines (9-12). Conversely, other NSCLC patients who were managed within the same health care system received speedier diagnosis and treatment. Given

this inequity and the complex interplay of patient, disease, and treatment factors which could potentially influence the timeliness of care for NSCLC patients, we sought to identify which factors were predictive of delays in order to help guide future quality improvement initiatives for NSCLC care.

Methods

Patient Population and Data Sources

The procedure used for data abstraction and quantification of time intervals for NSCLC diagnosis and treatment for this study cohort has been previously described (Chapter 2). In summary, all cases of pathologically confirmed, stage I to III (AJCC 6th ed.) NSCLC diagnosed and treated in Alberta, Canada (a population of approximately four million persons) from 2004 to 2011 were identified using the Alberta Cancer Registry. Patients were excluded from the study if they had a malignancy within 5 years prior to their NSCLC diagnosis (with exception of non-melanoma skin cancer), if medical records were unavailable for imputation of missing data, or if they received any of their diagnostic or treatment procedures outside of Alberta.

Patient, disease, and treatment variables as well as the dates of relevant diagnostic and treatment procedures necessary to define care intervals were obtained using linked administrative databases (Alberta Cancer Registry, provincial physician billing data, provincial inpatient/outpatient hospital data, and federal census data). The following variables were abstracted from the Alberta Cancer Registry: age at diagnosis, gender, habitational status (living alone versus not living alone), region of residence at diagnosis, TNM stage at diagnosis (AJCC 6th ed), NSCLC pathological subtype, first treatment modality, and year of diagnosis. Provincial physician billing data and provincial inpatient/outpatient hospital databases were used to

determine the total number of biopsy attempts prior to obtaining a diagnosis, biopsy modality (non-operative biopsy only (sputum cytology, thoracentesis, Image guided biopsy, or lymph node biopsy), operative biopsy only (bronchoscopy, mediastinoscopy, or pleural biopsy), or both non-operative and operative biopsies), all comorbid conditions diagnosed or treated within 1 year of the NSCLC diagnosis date were abstracted in order to calculate the Charlson comorbidity score (13, 14), and the acuity level of patient presentation (patients were deemed to have high acuity presentations for purposes of this study if they either: 1) required inpatient admission for 96 hours or longer within 30 days of their diagnosis; or 2) were diagnosed or treated for a pulmonary embolism or pneumonia within 30 days of diagnosis). Since individual patient data were not available in order to quantify levels of patient education and income, federal census data was used to ascertain aggregate values for education level (prevalence of high school diploma) and income level (median household income) for the postal code of the patient's residence at the time of diagnosis. Missing data were manually abstracted from the Cancer Control Alberta electronic medical record and/or paper charts.

Care Path Time Interval Definitions

Three time intervals were quantified for each patient as depicted in Figure 2.1. The Diagnostic Interval (DI) spanned from the date of the last chest x-ray which immediately preceded the first CT-scan of the thorax prior to the first attempt at tissue biopsy to the date of the diagnostic biopsy procedure which provided the pathological diagnosis. The treatment interval (TI) spanned from the date of the diagnostic biopsy procedure which provided the pathological diagnosis to the first day of treatment. The system interval (SI) spanned from the beginning of the DI to the

end of the TI. For patients who declined oncologic treatment, the date of their first oncologist consultation was used in lieu of the date of the first day of treatment in order to calculate the TI.

Analysis

Distributions of patient characteristics overall and greater than the median of each time interval of interest were calculated. Chi-square tests were performed to assess for significant differences in proportions of patients experiencing delayed intervals within the categories of each patient factor assessed. Multivariable logistic regression was performed in order to assess the association between patient, disease, and treatment factors and protracted system, diagnostic and treatment intervals. Since the median system (78 days), diagnostic (38 days), and treatment intervals (51 days) for the cohort were all observed to be longer than both local and international benchmarks for lung cancer care (9-11, 15), the median values for each of these intervals were used to dichotomize the cohort into those with and those without protracted intervals for each regression model. Therefore, system intervals of ≥78 days, diagnostic intervals of ≥38 days, and treatment intervals of ≥51 days were considered to be "delayed" for purposes of this analysis. The STATA 12 statistical software package (College Station, Texas) was used to conduct all analyses.

The following explanatory variables were assessed in the logistic regression model: age category at diagnosis (arbitrary cutpoints of: < 60, 60 to <70, 70 to <80 and ≥ 80 years), gender, habitational status (living alone versus not living alone) , Charlson comorbidity score (0, 1 or ≥ 2), acuity level of patient presentation (high acuity versus low acuity), region of residence at diagnosis, education level (quartile), income level (quartile), TNM stage at diagnosis (AJCC 6th ed), NSCLC pathological subtype, first treatment modality, total number of biopsy attempts (0 to

1, 2, or ≥3), biopsy modality (non-operative biopsy only, operative biopsy only, or both non-operative and operative biopsies), and year of diagnosis. Due to the number of variables assessed in each logistic regression model, a Bonferroni correction (0.05/47) was employed in order to reduce the identification of false positive associations. Thus, for purposes of discussion, only associations with corresponding p-values ≤0.001 were considered to be statistically significant.

Results

Between 2004 and 2011, 3,009 patients with biopsy confirmed NSCLC were diagnosed and treated in Alberta that met all study eligibility criteria. Table 3.1 summarizes patient demographic and clinical characteristics of interest at baseline. The median age at diagnosis was 69 years (range 38 to 95) and males accounted for 54% of the cohort. The stage distribution of the cohort was skewed towards those with locally advanced disease as follows: Stage I (28.9%); stage II (8.9%); stage III (62.2%). Most patients (64.3%) had at least one significant medical comorbidity (Charlson score ≥1). Adenocarcinoma (41.1%) and squamous cell carcinoma (34.7%) were the two most common NSCLC pathological subtypes.

The most common first modality of treatment was radiotherapy (42.6%) followed by surgery (28%), supportive care (19.2%) and chemotherapy (10.2%). Most patients (87.2%) required ≤2 biopsy procedures in order to establish their pathological diagnosis. High acuity presentations for diagnosis and care were observed in 30.3% of patients.

Tables 3.2, 3.3, and 3.4 summarize the results of the multivariable logistic regression models for the odds of having experienced protracted system, diagnostic, or treatment intervals respectively.

Influence of patient factors

A moderate but significant association was observed between older age categories at diagnosis and increased odds of experiencing delays across all three time intervals after adjusting for potential confounding factors. This association was most pronounced in the system interval whereby those age 60 to <70 and 70 to <80 at the time of diagnosis had 54% and 73% higher odds of experiencing system interval delays when compared to those younger than 60 years of age (P<0.0001). For patients ≥ 80 years of age at diagnosis, the association with delayed system interval was weaker than for those age 60 to < 70 and 70 to <80 and did not reach pre-specified levels of statistical significance (OR = 1.44, p=0.015).

Patients who lived alone at the time of diagnosis had higher odds of experiencing delayed diagnostic intervals when compared to those with a spouse (OR = 1.31, p<0.001). This association, however, was not apparent for either the treatment or system intervals.
Gender, comorbidity levels, and socioeconomic variables (income quartile, and education level quartile) were not observed to significantly increase the odds of experiencing any delay.
Region of residence at time of diagnosis did not increase the odds of experiencing delayed treatment or system intervals. Of note, after multivariable adjustment, patients from the sparsely populated Northern region were found to have lower odds of experiencing delayed diagnostic

workups when compared to those in the metropolitan region of Edmonton (OR = 0.48, $p<0.0001$).

Influence of Disease Factors

The presence of locally advanced (stage III) disease at diagnosis acted as a moderate protective factor against the odds of experiencing delays in all three time intervals with an OR for delayed system interval of 0.42 ($P<0.0001$).

Having a high acuity presentation at the time of diagnosis also acted as a strong protective factor against experiencing any delays, especially diagnostic delays (OR = 0.34, $p<0.0001$). Histopathological subtype of NSCLC did not consistently predict for increased odds of having delayed intervals for diagnosis or treatment.

Influence of Treatment Factors

Patients who received treatments other than supportive care had higher odds of delayed treatment and system intervals. This association was strongest for patients treated surgically for whom the adjusted odds of experiencing delayed treatment (OR = 5.12, $p<0.0001$) and system intervals (OR = 5.23, $p<0.0001$) were much higher than those who were managed with supportive care. Modality of first treatment was not observed to influence the odds of experiencing a delayed diagnostic interval after adjustment for potential confounding factors.

A dose response gradient was observed with respect to the odds of experiencing protracted diagnostic intervals and the number of biopsy attempts required to achieve the diagnosis

whereby patients who needed 2 (OR = 3.18, $p<0.0001$) or ≥3 biopsies (OR = 9.82, $p<0.0001$) had considerably higher odds of experiencing diagnostic delays than patients whose diagnosis was established with a single biopsy attempt. Weaker and inconsistent associations were observed between the modality of diagnostic biopsies used and the odds of experiencing a delay. The total number of biopsy attempts required in order to obtain a diagnosis, therefore, predicted diagnostic delays better than the modality of the biopsies used to obtain the diagnosis.

Discussion

The aim of this study was to identify which patient, disease, and treatment factors were associated with increased probability of experiencing delayed diagnostic, treatment and system intervals for NSCLC management in Alberta. A main finding of this study was that having surgery as the first modality of treatment considerably increased the odds of experiencing delayed treatment and system intervals. By contrast, three variables acted as protective factors against delayed diagnostic, treatment or system intervals: 1) having locally advanced (stage III) disease; 2) a high acuity presentation; and 3) age <60 at the time of diagnosis. In other words, younger patients with locally advanced disease who presented with high acuity symptoms that were not surgical candidates experienced the most prompt journey through the system. Ironically, this stratum of patients also has the smallest probability of achieving a cure for their disease while also incurring the most expensive diagnostic workups due to inpatient admission for diagnosis and care. Furthermore, given the finite resources available to a publicly funded and administered health care system, the swift journey of these patients may have contributed to the delays of other NSCLC patients with earlier stage disease who possess a significantly better chance of achieving a cure.

How is this type of inequality rectified? Unfortunately, there is no easy remedy for this conundrum as it is largely a product of the skewed stage distribution which arises in the absence of population based screening for lung cancer. Moving the NSCLC stage distribution towards earlier stage disease through the use of population based screening should decrease the number of locally advanced presentations and therefore reduce the heavy economic costs associated with high acuity inpatient admissions while also improving the overall survival for NSCLC. Presently, efforts are underway to study how to best employ low-dose CT screening examinations in Alberta; however the implementation of population based screening programs remains years away.

In the absence of any immediate plans to implement CT based screening on the population level, efforts to minimize the risk of unnecessary treatment and system delays in Alberta should focus on streamlining the care for patients who require surgery. The excess odds of treatment delays for surgical patients most likely arise from two possible causes. Firstly, all surgical patients require a sequence of staging and performance status assessments in order to be deemed operative candidates after their diagnosis has been established. These tests typically include pulmonary function testing, mediastinal lymph node assessments, anesthesia consultations (including cardiac risk assessments), and further imaging scans (PET, CT imaging). Guiding a patient through these pre-operative assessments requires constant coordination, dynamic oversight, and patient advocacy – all of which consume time and energy. During the study era, supervision of this process was largely left to individual surgeons who have limited time and

resources. This approach was therefore likely suboptimal for ensuring that each patient navigated the system as quickly as possible.

Several groups have reported success in shortening care intervals while simultaneously producing cost savings for NSCLC cancer care through the use of nursing navigators (16-18). Similarly, our study found indirect evidence of the beneficial impact of nursing navigators. The timelier diagnostic intervals for Northern Albertan patients in this study are likely due, in part, to the efforts of First Nation's patient nursing navigators who, during the study period, would routinely arrange for streamlined interdisciplinary assessments in rapid succession in tertiary care facilities for patients with suspected lung cancer that lived in smaller Northern Alberta communities. Thus, nursing navigation represents a potential remedy to reduce the likelihood of the delays which were prevalent during the study period for surgical patients. In December of 2011, the Alberta Thoracic Oncology Program (ATOP) was created in order to address delays in NSCLC care (11). A key feature of ATOP was to improve coordination of care for NSCLC diagnosis and treatment through the use of centralized nursing navigators which has likely already resulted in reduced waiting times for a considerable proportion of NSCLC patients in Alberta.

Secondly, NSCLC patients who require surgical care need to wait for operating room time, which is predictably in short supply. A notable limitation of this study was its inability to subdivide the treatment interval into its component interim intervals, the pre-operative interval (interval from diagnosis date to completion of all pre-treatment assessments) and the operative room waiting interval (the interval from completion of all pre-operative assessments to the surgery date), as administrative data does not reliably capture each pre-operative assessment. As

such, further study is required in order to determine the impact of limited operating room time on the likelihood of experiencing delayed system and treatment intervals for NSCLC patients in Alberta.

This study found no evidence to indicate that patients with lower socioeconomic status (SES) received less timely care when compared to higher SES strata of NSCLC patients after adjusting for confounding factors. These findings are consistent with other published studies which have examined the impact of socioeconomic factors on the timelines for care of lung cancer patients which (19-22) have failed to find a significant association between lower SES and delayed care. Our findings should, however be taken with caution as the use of aggregate values for income and educational variables may have had the effect of obscuring or rendered nil any potential association between lower SES and NSCLC delayed care. As well, our study was unable to assess the impact of other SES factors such as race or occupation given the limitations of our data sources.

This study found an intuitive relationship between the total number of biopsies required for achieving a diagnosis and an increased likelihood of experiencing all delays whereby those who had ≥3 biopsies had the greatest likelihood of experiencing a delayed system or diagnostic interval. This is due, in part, to the commonly used strategy of obtaining biopsies in a "serial" sequence whereby a biopsy procedure is performed and the pathological specimen is processed (which typically takes several weeks), and it is only until after a sample has been deemed non-diagnostic that a repeat biopsy procedure is ordered. Furthermore, during the study period, there were no Alberta-specific evidence-based guidelines in place which served to guide the choice of first biopsy modality for a given presentation of suspected NSCLC therefore leaving the choice of first biopsy modality at the discretion of the first specialist who assessed the patient. Since

international diagnostic guidelines (23) now exist, which recommend which biopsy modality is appropriate as a first choice for particular subsets of patients with NSCLC, the development of similar evidence based guidelines for Albertan NSCLC patients may potentially improve a patient's chances of obtaining a diagnosis with the least number of biopsy procedures and therefore shorten their diagnostic and system intervals. An alternative approach to obtaining a tissue diagnosis may be to obtain multiple "parallel" biopsy procedures at the outset (for example a bronchoscopy and a CT guided biopsy) for those for whom tissue diagnoses are known to routinely require more than one biopsy attempt (such as patients with smaller peripheral tumours (23)). This approach is potentially costly, could expose patients to more material risks and could even increase the backlog of patients waiting for diagnostic procedures, but may nonetheless warrant further analysis and consideration.

Conclusion

The primary factors influencing the probability of delays in the diagnosis and treatment of NSCLC in decreasing order of importance were: first treatment modality, acuity level of presentation, stage, and age. The results of this study suggest that care intervals could be shortened for NSCLC patients through the use of streamlined coordination of care, especially for those who require surgery.

References

1. Cancer fact sheet [homepage on the Internet]. Geneva, Switzerland: World Health Organization. 2014 February 2014. Available from: http://www.who.int/mediacentre/factsheets/fs297/en/.

2. Canadian Partnership Against Cancer. Lung cancer in canada: A supplemental system performance report. Toronto: Canadian Partnership Against Cancer; 2010.

3. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian cancer statistics 2014. Toronto, Ontario: Canadian Cancer Society; 2014.

4. Risberg T, Sorbye SW, Norum J, Wist EA. Diagnostic delay causes more psychological distress in female than in male cancer patients. Anticancer Res. 1996 Mar-Apr;16(2):995-9.

5. O'Rourke N, Edwards R. Lung cancer treatment waiting times and tumour growth. Clin Oncol (R Coll Radiol). 2000;12(3):141-4.

6. Buccheri G, Ferrigno D. Lung cancer: Clinical presentation and specialist referral time. Eur Respir J. 2004 Dec;24(6):898-904.

7. Kanashiki M, Satoh H, Ishikawa H, Yamashita YT, Ohtsuka M, Sekizawa K. Time from finding abnormality on mass-screening to final diagnosis of lung cancer. Oncol Rep. 2003 May-Jun;10(3):649-52.

8. Kashiwabara K, Koshi S, Itonaga K, Nakahara O, Tanaka M, Toyonaga M. Outcome in patients with lung cancer found on lung cancer mass screening roentgenograms, but who did not subsequently consult a doctor. Lung Cancer. 2003 Apr;40(1):67-72.

9. Jakobsen E, Green A, Oesterlind K, Rasmussen TR, Iachina M, Palshof T. Nationwide quality improvement in lung cancer care: The role of the danish lung cancer group and registry. J Thorac Oncol. 2013 Oct;8(10):1238-47.

10. BTS recommendations to respiratory physicians for organising the care of patients with lung cancer. the lung cancer working party of the british thoracic society standards of care committee. Thorax. 1998 Jun;53 Suppl 1:S1-8.

11. Alberta Health Services. Program to deliver faster treatment for lung cancer patients. News Release. Calgary, Alberta: Alberta Health Services; 2011 16 December 2011.

12. Alberts WM, Bepler G, Hazelton T, Ruckdeschel JC, Williams JH,Jr, American College of Chest Physicians. Lung cancer. practice organization. Chest. 2003 Jan;123(1 Suppl):332S-7S.

13. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis. 1987;40(5):373-83.

14. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the charlson comorbidity index predicted in-hospital mortality. J Clin Epidemiol. 2004 Dec;57(12):1288-94.

15. Alberts WM, Bepler G, Hazelton T, Ruckdeschel JC, Williams JH,Jr, American College of Chest Physicians. Lung cancer. practice organization. Chest. 2003 Jan;123(1 Suppl):332S-7S.

16. Hunnibell LS, Rose MG, Connery DM, Grens CE, Hampel JM, Rosa M, et al. Using nurse navigation to improve timeliness of lung cancer care at a veterans hospital. Clin J Oncol Nurs. 2012 Feb;16(1):29-36.

17. Alsamarai S, Yao X, Cain HC, Chang BW, Chao HH, Connery DM, et al. The effect of a lung cancer care coordination program on timeliness of care. Clin Lung Cancer. 2013 Sep;14(5):527-34.

18. Wagner EH, Ludman EJ, Aiello Bowles EJ, Penfold R, Reid RJ, Rutter CM, et al. Nurse navigators in early cancer care: A randomized, controlled trial. J Clin Oncol. 2014 Jan 1;32(1):12-8.

19. Bardell T, Belliveau P, Kong W, Mackillop WJ. Waiting times for cancer surgery in ontario: 1984-2000. Clin Oncol (R Coll Radiol). 2006 Jun;18(5):401-9.

20. Simunovic M, Theriault ME, Paszat L, Coates A, Whelan T, Holowaty E, et al. Using administrative databases to measure waiting times for patients undergoing major cancer surgery in ontario, 1993-2000. Can J Surg. 2005 Apr;48(2):137-42.

21. Johnston GM, MacGarvie VL, Elliott D, Dewar RA, MacIntyre MM, Nolan MC. Radiotherapy wait times for patients with a diagnosis of invasive cancer, 1992-2000. Clin Invest Med. 2004 Jun;27(3):142-56.

22. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Impact of deprivation and rural residence on treatment of colorectal and lung cancer. Br J Cancer. 2002 Sep 9;87(6):585-90.

23. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American college of chest physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e142S-65S.

Table 3.1 – Patient Characteristics at Diagnosis

Characteristic	n (%)
Age	
<60	618 (20.5)
60 to <70	907 (30.1)
70 to <80	1,036 (34.4)
≥80	448 (14.9)
Stage (AJCC 6th ed)	
I	869 (28.9)
II	268 (8.9)
III	1,872 (62.2)
Gender	
Female	1,383 (46.0)
Male	1,626 (54.0)
Health Region At Diagnosis	
Edmonton	1,062 (35.3)
South Zone	269 (8.9)
Calgary Zone	919 (30.5)
Central Zone	433 (14.4)
North Zone	326 (10.8)
Lives Alone	
No	1,661 (55.2)
Yes	1,348 (44.8)
Charlson Comorbidity Score	
0	1,076 (35.8)
1	1,176 (39.1)
≥ 2	757 (25.2)
NSCLC Subtype	
Adenocarcinoma	1,239 (41.1)
Large Cell Carcinoma	110 (3.7)
NSCLC NOS	615 (20.4)
Squamous Cell Carcinoma	1,045 (34.7)
First Treatment Modality	
Supportive Care	578 (19.2)
Radiotherapy	1,281 (42.6)
Chemotherapy	307 (10.2)
Surgery	842 (28.0)
High Acuity Presentation	
No	2,097 (69.7)
Yes	912 (30.3)
Total Biopsy Attempts	
0-1	1,665 (55.3)
2	960 (31.9)
≥ 3	384 (12.8)
Biopsy Modality	
Non-Operative Biopsy Only	1,041 (35.5)
Operative Biopsy Only	702 (23.9)
Both Non-Operative & Operative Biopsy	1,190 (40.6)

Year of Diagnosis	
2004-2005	650 (21.6)
2006-2007	770 (25.6)
2008-2009	772 (25.7)
2010-2011	817 (27.2)
Income Quartile	
(0 < $43,365)	743 (24.9)
($43,365 < $56,366)	746 (25.0)
($56,366 < $74,645)	745 (25.0)
(≥ $74,645)	745 (25.0)
Education Level	
(Prevalence of High School Diploma)	
1st quartile	744 (25)
2nd quartile	738 (24.8)
3rd quartile	751 (25.2)
4th quartile	746 (25.0)

Table 3.2 – Adjusted Odds Ratios of Protracted System Interval (≥78 days)

Characteristic	n (%) in category with SI ≥ 78 Days	Adjusted OR (95%CI)	p-value
Age	p <0.0001		
<60	287 (46.4)	Reference	-
60 to <70	488 (53.8)	1.54 (1.22 to 1.95)	<0.0001
70 to <80	550 (53.9)	1.73 (1.36 to 2.19)	<0.0001
≥80	192 (42.8)	1.44 (1.07 to 1.94)	0.015
Stage (AJCC 6th ed)	p <0.0001		
I	593 (68.2)	Reference	-
II	184 (68.7)	0.89 (0.64 to 1.24)	0.501
III	740 (39.5)	0.42 (0.33 to 0.53)	<0.0001
Gender	p = 0.017		
Female	730 (52.8)	Reference	-
Male	787 (48.4)	0.90 (0.76 to 1.07)	0.243
Health Region	p = 0.047		
Edmonton Zone	539 (50.8)	Reference	-
South Zone	140 (52.0)	1.23(0.90 to 1.69)	0.192
Calgary Zone	465 (50.6)	1.00 (0.81 to 1.23)	0.981
Central Zone	233 (53.8)	1.28 (0.98 to 1.67)	0.067
North Zone	140 (42.9)	0.66 (0.49 to 0.90)	0.008
Lives Alone	p = 0.363		
No	825 (49.7)	Reference	-
Yes	692 (51.3)	1.15(0.96 to 1.36)	0.124
Charlson Score	p = 0.006		
0	566 (52.6)	Reference	-
1	607 (51.6)	1.07 (0.8 to 1.30)	0.474
≥ 2	344 (45.4)	1.09 (0.87 to 1.37)	0.452
NSCLC Subtype	p <0.0001		
Adenocarcinoma	705 (56.9)	Reference	-
Large Cell Carcinoma	51 (46.4)	0.45 (0.29 to 0.71)	0.001
NSCLC NOS	260 (42.3)	0.80 (0.64 to 1.01)	0.060
Squamous Cell Carcinoma	501 (47.9)	0.76 (0.62 to 0.92)	0.006
First Treatment Modality	p <0.0001		
Supportive Care	158 (27.3)	Reference	-
Radiotherapy	594 (46.4)	2.52 (1.98 to 3.20)	<0.0001
Chemotherapy	141 (45.9)	2.84 (2.05 to 3.92)	<0.0001
Surgery	624 (74.1)	5.23 (3.87 to 7.09)	<0.0001
High Acuity Presentation	p <0.0001		
No	1224 (58.4)	Reference	-
Yes	293 (32.1)	0.43 (0.36 to 0.52)	<0.0001
Total Biopsy Attempts	p <0.0001		
0-1	827 (49.7)	Reference	-
2	458 (47.7)	1.53 (1.05 to 2.23)	0.026
≥3	232 (60.4)	3.16 (2.03 to 4.91)	<0.0001

Biopsy Modality	p =0.371		
Non-Operative Biopsy Only	510 (49.0)	Reference	-
Operative Biopsy Only	368 (52.4)	1.19 (0.95 to 1.49)	0.138
Both Non-Operative & Operative	597 (50.2)	0.68 (0.45 to 1.00)	0.053
Year of Diagnosis	p = 0.054		
2004-2005	304 (46.8)	Reference	-
2006-2007	380 (49.4)	1.10 (0.87 to 1.39)	0.425
2008-2009	416 (53.9)	1.27 (1.00 to 1.61)	0.051
2010-2011	417 (51.0)	1.14 (0.90 to 1.45)	0.275
Income Quartile	p = 0.219		
(0 < $43,365)	352 (47.4)	Reference	-
($43,365 < $56,366)	378 (50.7)	1.00 (0.79 to 1.27)	0.989
($56,366 < $74,645)	382 (51.3)	1.09 (0.85 to 1.39)	0.496
(≥ $74,645)	392 (52.6)	1.01 (0.77 to 1.33)	0.920
Education Level*	p = 0.062		
Lowest quartile	358 (48.1)	Reference	-
2nd quartile	358 (48.5)	0.89 (0.70 to 1.13)	0.334
3rd quartile	408 (54.3)	1.21 (0.94 to 1.56)	0.145
Highest quartile	380 (50.9)	0.94 (0.70 to 1.25)	0.663

*Prevalence of high school diplomas for the patient's postal code at the time of diagnosis

Table 3.3: Adjusted Odds Ratios of Protracted Diagnostic Interval (≥38 days)

Characteristic	n (%) in category with DI ≥ 38 Days	Adjusted OR (95%CI)	p-value
Age	p = 0.276		
<60	299 (48.4)	-	-
60 to <70	438 (48.3)	1.04 (0.83 to 1.31)	0.710
70 to <80	531 (51.3)	1.22 (0.97 to 1.54)	0.085
≥80	237 (52.9)	1.41 (1.06 to 1.87)	0.019
Stage (AJCC 6th ed)	p <0.0001		
I	540 (62.1)	-	-
II	145 (54.1)	0.68 (0.50 to 0.92)	0.012
III	820 (43.8)	0.54 (0.44 to 0.68)	<0.0001
Gender	p = 0.046		
Female	719 (52.0)	-	-
Male	786 (48.3)	0.97 (0.82 to 1.14)	0.705
Health Region	p <0.0001		
Edmonton Zone	568 (53.5)	-	-
South Zone	115 (42.8)	0.64 (0.47 to 0.87)	0.005
Calgary Zone	500 (54.4)	1.03 (0.84 to 1.26)	0.785
Central Zone	199 (46.0)	0.76 (0.59 to 0.98)	0.035
North Zone	123 (37.7)	0.48 (0.36 to 0.65)	<0.0001
Lives Alone	p = 0.002		
No	789 (47.5)	-	-
Yes	716 (53.1)	1.31 (1.11 to 1.55)	0.001
Charlson Score	p = 0.692		
0	540 (50.2)	-	-
1	578 (49.2)	1.01 (0.84 to 1.21)	0.936
≥ 2	387 (51.1)	1.36 (1.10 to 1.70)	0.006
NSCLC Subtype	p = 0.001		
Adenocarcinoma	673 (54.3)	-	-
Large Cell Carcinoma	52 (47.3)	0.68 (0.44 to 1.05)	0.084
NSCLC NOS	286 (46.5)	0.86 (0.69 to 1.08)	0.200
Squamous Cell Carcinoma	494 (47.3)	0.80 (0.66 to 0.97)	0.230
First Treatment Modality	p <0.0001		
Supportive Care	254 (43.9)	-	-
Radiotherapy	604 (47.2)	1.06 (0.84 to 1.32)	0.636
Chemotherapy	137 (44.6)	1.11 (0.81 to 1.52)	0.526
Surgery	510 (60.6)	1.35 (1.01 to 1.80)	0.042
High Acuity Presentation	p <0.0001		
No	1,198 (57.1)	-	-
Yes	307 (33.7)	0.34 (0.28 to 0.41)	<0.0001
Total Biopsy Attempts	p <0.0001		
0-1	752 (45.2)	-	-
2	479 (49.9)	3.18 (2.16 to 4.67)	<0.0001
≥3	274 (71.4)	9.82 (6.20 to 15.57)	<0.0001
Biopsy Modality	p = 0.002		
Non-Operative Biopsy Only	482 (46.3)	-	-
Operative Biopsy Only	350 (49.9)	1.17 (0.94 to 1.45)	0.167
Both Non-Operative & Operative	641 (53.9)	0.41 (0.28 to 0.62	<0.0001

Year of Diagnosis	p = 0.129		
2004-2005	339 (52.2)	-	-
2006-2007	375 (48.7)	0.78 (0.62 to 0.99)	0.039
2008-2009	404 (52.3)	0.82 (0.65 to 1.04)	0.101
2010-2011	387 (47.4)	0.72 (0.57 to 0.91	0.005
Income Quartile	p = 0.047		
(0 < $43,365)	344 (46.3)	-	-
($43,365 < $56,366)	384 (51.5)	1.24 (0.99 to 1.57)	0.063
($56,366 < $74,645)	370 (49.7)	1.11 (0.87 to 1.40)	0.409
(≥ $74,645)	397 (53.3)	1.17 (0.90 to 1.53)	0.246
Education Level*	p = 0.012		
Lowest quartile	338 (45.4)	-	-
2nd quartile	369 (50.0)	1.02 (0.81 to 1.29)	0.872
3rd quartile	388 (51.7)	1.00 (0.78 to 1.28)	0.986
Highest quartile	400 (53.6)	0.94 (0.71 to 1.24)	0.665

*Prevalence of high school diplomas for the patient's postal code at the time of diagnosis

Table 3.4 –Adjusted Odds Ratios of Protracted Treatment Interval (≥51 days)

Characteristic	n (%) in category with TI ≥ 51 Days	Adjusted OR (95%CI)	p-value
Age	p < 0.0001		
<60	274 (45.7)	Reference	-
60 to <70	477 (54.8)	1.56 (1.24 to 1.98)	<0.0001
70 to <80	505 (52.3)	1.50 (1.19 to 1.80)	0.001
≥80	163 (43.6)	1.22 (0.90 to 1.66)	0.191
Stage (AJCC 6th ed)	p < 0.0001		
I	554 (66.4)	Reference	-
II	173 (65.8)	0.70 (0.70 to 1.32)	0.785
III	692 (40.4)	0.38 (0.38 to 0.60)	<0.0001
Gender	p = 0.120		
Female	676 (52.1)	Reference	-
Male	743 (49.1)	0.93 (0.79 to 1.11)	0.445
Health Region	p <0.043		
Edmonton Zone	476 (48.1)	Reference	-
South Zone	134 (56.8)	1.42 (1.02 to 1.97)	0.035
Calgary Zone	448 (50.9)	1.06 (0.86 to 1.31)	0.563
Central Zone	214 (54.5)	1.21 (0.93 to 1.59)	0.159
North Zone	147 (47.3)	0.86 (0.64 to 1.17)	0.341
Lives Alone	p = 0.889		
No	792 (50.4)	Reference	-
Yes	627 (50.7)	1.02 (0.86 to 1.21)	0.836
Charlson Score	p < 0.0001		
0	554 (53.7)	Reference	-
1	576 (51.7)	1.06 (0.88 to 1.28)	0.545
≥ 2	289 (43.6)	0.89 (0.71 to 1.12)	0.323
NSCLC Subtype	p <0.0001		
Adenocarcinoma	649 (56.1)	Reference	-
Large Cell Carcinoma	57 (53.8)	0.67 (0.43 to 1.04)	0.079
NSCLC NOS	230 (40.5)	0.77 (0.61 to 0.97)	0.024
Squamous Cell Carcinoma	483 (49.3)	0.85 (0.69 to 1.03)	0.104
First Treatment Modality	p <0.0001		
Supportive Care	89 (23.4)	Reference	-
Radiotherapy	599 (46.8)	3.61 (2.72 to 4.80)	<0.0001
Chemotherapy	124 (46.3)	3.58 (2.50 to 5.12)	<0.0001
Surgery	1,419 (50.5)	5.12 (3.68 to 7.13)	<0.0001
High Acuity Presentation	p <0.0001		
No	1,140 (56.4)	Reference	-
Yes	279 (35.4)	0.55 (0.46 to 0.67)	<0.0001
Total Biopsy Attempts	p <0.0001		
0-1	862 (55.7)	Reference	-
2	416 (46.3)	0.59 (0.40 to 0.86)	0.006
≥3	141 (38.8)	0.43 (0.28 to 0.67)	<0.0001
Biopsy Modality	p < 0.0001		
Non-Operative Biopsy Only	539 (57.5)	Reference	-
Operative Biopsy Only	325 (48.3)	0.67 (0.53 to 0.84)	0.001
Both Non-Operative & Operative	499 (44.4)	1.09 (0.73 to 1.62)	0.677

Year of Diagnosis	p = 0.162		
2004-2005	297 (48.3)	Reference	-
2006-2007	351 (48.5)	0.97 (0.76 to 1.23)	0.733
2008-2009	389 (53.4)	1.25 (0.99 to 1.59)	0.064
2010-2011	382 (51.4)	1.08 (0.85 to 1.38)	0.523
Income Quartile	p = 0.596		
(0 < $43,365)	330 (48.7)	Reference	-
($43,365 < $56,366)	361 (52.2)	1.01 (0.80 to 1.29)	0.905
($56,366 < $74,645)	353 (50.1)	0.98 (0.76 to 1.25)	0.852
(≥ $74,645)	366 (51.5)	0.96 (0.73 to 1.27)	0.787
Education Level*	p = 0.531		
Lowest quartile	350 (50.9)	Reference	-
2nd quartile	331 (48.5)	0.82 (0.64 to1.05)	0.108
3rd quartile	360 (50.8)	1.01 (0.78 to 1.31)	0.925
Highest quartile	369 (52.4)	1.02 (0.76 to 1.36)	0.921

*Prevalence of high school diplomas for the patient's postal code at the time of diagnosis

Chapter 4: Discussion

Summary of Findings

This study represents the first systematic effort to quantify the distribution of time intervals experienced along the NSCLC diagnostic and treatment care paths at the population level for a contemporary cohort of patients treated with surgery, radiotherapy, chemotherapy, or best supportive care in Alberta.

With respect to the primary aim of this study, the median values for the diagnostic, treatment, and system intervals for the entire cohort were found to be 38 (95%CI 36-40), 51 (95%CI 49-53), 78 (95% CI 76-80) days respectively. At the 75th percentile level, the diagnostic, treatment, and system intervals were 78 (95% CI 74-82), 82 (95%CI 79-85), and 123 (95% CI 119-126) days respectively. Due to the use of proxy dates, the estimates of the Diagnostic and System intervals which were calculated for this study are almost certainly underestimations of the true durations of the care intervals experienced by these patients. Regardless, during the study period, patients in our cohort waited longer than both local (1) and international (2-4) prescribed guidelines for the timeliness of NSCLC diagnosis and treatment. Overall, the largest component of the system interval (i.e. the tightest bottle neck) was found to be the treatment interval and the largest component of the diagnostic interval was determined to be the diagnostic biopsy interval. When stratified by first treatment modality, patients treated surgically were found to have the longest diagnostic (both diagnostic imaging and diagnostic biopsy), treatment, and system intervals ($p<0.0001$).

The second aim of this study was to identify potential independent risk factors associated with increased odds of experiencing delayed diagnostic, treatment, or system intervals. A wide mixture of patient (age, gender, comorbidity levels, marital status), disease (TNM Stage, NSCLC Subtype), treatment (First treatment modality, acuity level of presentation, biopsy modality, total number of biopsy attempts, year of diagnosis), and socioeconomic (region of residence at diagnosis, income and education levels) variables were evaluated in the multivariable logistical regression analysis. After multivariable adjustment and taking into account a Bonferroni correction, age above 60, and treatment with modalities other than supportive care, especially surgery (OR for treatment delay = 5.23, $p<0.0001$) were associated with increased odds of experiencing delays. Factors associated with prompt care included high acuity presentations (OR for delayed diagnosis = 0.34, $p<0.0001$), and stage III disease (OR for delayed treatment = 0.38, $p<0.0001$).

Study Strengths and Limitations

The major strength of this study is its large, population-based, sample size of NSCLC patients (n=3009) which were identified by the Alberta Cancer Registry. The Alberta Cancer Registry is annually evaluated by the North American Association of Comprehensive Cancer Registries and has consistently achieved the highest level of certification (5). As such, our study's population represents essentially all biopsy confirmed, NSCLC cases (stage I to III) diagnosed and treated in Alberta during the study dates. This large sample size permitted the inclusion of a large number of potential explanatory variables in the multivariable model, reduced selection bias, allowed for wide generalizability and validity of the results, and reduced the effects of individual outliers on the overall results of the study. Furthermore, since the study period represented a contemporary

era (2004-2011), the patterns of practice and care paths which were examined in this study are largely identical to those in clinical use today and electronic medical records were available for convenient imputation of missing administrative data.

This study utilized internationally accepted guidelines, the Arhus Consensus statement (6) and Refined Anderson Model of Total Patient Delay (7), in order to select milestones along the NSCLC care path that served to define the beginning and end of each measured time interval. By doing so, this study will add to the international body of literature assessing the timeliness of diagnosis and treatment of NSCLC patients and should allow for inclusion in pooled meta-analytical endeavors.

Finally, efforts were made to exclude the possibility of a false positive association arising from the large number of comparisons which were performed in the multivariable analysis through the use of a Bonferroni correction. Thus, only variables with highly statistically significant association (p-values ≤ 0.001) were considered to be statistically significant for purposes of discussion.

The primary limitations of this study stem from its use of administrative medical databases. Since the hospital inpatient/outpatient and physician billing databases were not primarily designed for use in studies such as this, exposure variables gathered from these databases are potentially at risk of information bias. Such an information bias could take the form of misclassification of exposures which could arise due to either erroneous or unclear clinical documentation or even a misdiagnosis (8). It should be noted, however, that validation studies of data-linking analytical methods very similar to those employed for this study have found a high

level of accuracy of data obtained from provincially administered medical databases in Alberta, especially physician billing databases (9).

A second limitation of this study pertains to the possibility of an ecological fallacy with respect to some socioeconomic variables. Since socioeconomic variables are not routinely captured in the provincially administered healthcare databases utilized in this study, aggregate values for education level (prevalence of high school diploma or higher) and income (median household income) were obtained for each patient's postal code at the time of diagnosis. The use of these two aggregate values may have had the effect of obscuring any associations between socioeconomic exposures and delays in the multivariable analysis on the individual level in keeping with the ecological fallacy (10). It should, however, be noted that other studies which have assessed the impact of socioeconomic factors on the timeliness of NSCLC care have not demonstrated a clear association between lower socioeconomic status and NSCLC delays in developed nations (11-14) in keeping with the findings of this study.

A third limitation of this study stems from the inability of our administrative data, to reliably capture the date of symptom onset for individual patient. An ideal accounting of the diagnostic and system intervals for patients with NSCLC patients should begin with the date in which symptom were first experienced by the patient as stipulated in the Arhus consensus statement (6). Determination of this date is a complex task since initial symptoms associated with NSCLC may be vague in nature, can be attributable to commonly comorbid conditions, such as chronic obstructive pulmonary disorder, and are often initially ignored. For purposes of this study, the date of the last chest-x-ray which immediately preceded the CT scan of the chest prior to the first biopsy attempt was used as a proxy milestone to demarcate the beginning of the diagnostic and

system intervals. The use of this proxy milestone almost certainly had the effect of rendering our estimates for the diagnostic and system intervals shorter than what individual patients experienced in reality.

Policy Implications and Future Research

The findings of this study have established the contemporary benchmark durations for NSCLC diagnosis and treatment intervals in Alberta. Since these quantified benchmarks exceeded all prescribed guidelines for timeliness of NSCLC care, future research initiatives are warranted.

Firstly, quality improvement studies assessing the timeliness of care for NSCLC patients are now possible. As the end of the study period directly precedes the implementation of the Alberta Thoracic Oncology Program, our study results should be used for comparison with the "post-ATOP" era time intervals in order to determine if the ATOP program has been successful in reducing time intervals for NSCLC diagnosis and care in Alberta. These types of quality improvement and reporting initiatives should be repeated on an annual basis and should be done in the context of formal oversight by an arms-length Alberta Health Services appointed committee or working group. This would serve to ensure proper objectivity and unbiased reporting of progress, or lack thereof, in the reduction of care interval durations, and to critically appraise the impact of costly interventions, such as the allocation of more diagnostic biopsy procedures, in order to justify their continued funding. Given the high proportion of patients who experienced delayed care intervals in this study, Alberta must create institutional infrastructure with a mandate to regularly measure, compare, and report the durations of care intervals for NSCLC patients and to assess the efficacy of interventions aimed at reducing the duration of care intervals to ensure constant quality improvement of NSCLC care in Alberta.

Other countries, namely Denmark, have demonstrated significant improvements in overall survival of NSCLC patients after the implementation of quality improvement initiatives which featured the capture and reporting of diagnostic and treatment intervals on an annual basis as well as use of consensus guidelines which delineated optimal diagnostic and treatment care paths for patients with NSCLC. If Alberta is to make any gains in quality of care for NSCLC patients, it must do likewise.

Secondly, this study found that 44.7% of all NSCLC patients in Alberta had a non-diagnostic first biopsy attempt. Since each additional diagnostic biopsy attempt represents both a sharp increase in a patient's odds of experiencing delayed diagnostic intervals and significant additional monetary costs to the health care system, the development of strategies to reduce non-diagnostic first biopsy attempts is imperative. Presently, Alberta does not have evidence based guidelines which specify which biopsy modality affords the best opportunity for obtaining a diagnosis for a given imaging distribution of suspected NSCLC. As such, the choice of the modality of the first biopsy is at the discretion of the first specialist who assesses the patient which frequently results, as demonstrated by the findings of this study, in a non-diagnostic first biopsy. Further study is needed to characterize which patients are at highest risk of having multiple non-diagnostic biopsy attempts and strategies need to be developed in order to mitigate this unnecessary risk. A logical means to reduce the number of non-diagnostic biopsies performed in Alberta would be to direct the Alberta thoracic oncology community (respirologists, thoracic surgeons, medical oncologists, radiation oncologists, interventional radiologists, and pathologists) to produce consensus, evidenced based, clinical guidelines which specify a diagnostic algorithm that includes recommendations of which biopsy modality should

be used first for a given radiological distribution of suspected NSCLC. Other thoracic oncology communities, such as the American Society of Chest Physicians, have successfully generated consensus guidelines (15) to help guide physicians in the establishment of a diagnosis of lung cancer, and Alberta, for the aforementioned reasons, should follow suit.

Thirdly, since first treatment with surgery was strongly associated with higher odds of receiving delayed treatment, further evaluation of the treatment interval for surgical patients is necessary. Interim intervals for surgical treatment including the pre-operative interval (time interval from diagnosis date to the completion of all pre-operative assessments) and the operating room waiting interval (interval from completion of all pre-operative assessments to the surgery date) should be quantified and assessed in order to identify potentially modifiable bottlenecks for surgically treated NSCLC patients.

Finally, our study found evidence of the presence of a "waiting times paradox" whereby patients with locally advanced disease (who have the lowest chances of a cure) had the swiftest journey through the system while those with early stage disease (who have the highest chance of a cure) had the most protracted course through the system. A follow-up study is therefore planned which will assess the impact of this "waiting times paradox" on stage specific survival; effort will be made to adjust for known confounding factors (patient, treatment, and disease factors). As well, the presence of this "waiting times paradox" amongst NSCLC patients in Alberta needs to be addressed at a provincial level in order to ensure that the rapid care of patients with locally advanced disease does not prolong the care paths of patients with earlier stage disease or jeopardize their opportunities to receive prompt curative treatment.

Conclusion

Albertans with Stage I to III NSCLC experienced considerably long intervals for their diagnosis and treatment which exceeded both local and international prescribed guidelines. The largest component of the system interval for all NSCLC care was found to be the treatment interval. The primary factors influencing the probability of delays in the diagnosis and treatment of NSCLC in decreasing order of importance were: first treatment modality, acuity level of presentation, stage, and age. The findings of this study have several key policy implications. Firstly, further quality improvement studies and robust data reporting infrastructure are needed in order to ensure that measures aimed at shortening care intervals are achieving their stated goals and to drive future quality improvement initiatives for NSCLC care in Alberta. Secondly, evidenced based, Alberta specific guidelines should be developed in order to guide the optimal choice of a first diagnostic biopsy modality to reduce the high proportion of patients with non-diagnostic first biopsies attempts. Thirdly, the treatment intervals of surgical patients must be streamlined through the use of enhanced coordination of care and further assessment of the impact of protracted operating room waiting intervals on the risk of delayed care intervals.

References

1. Alberta Health Services. Program to deliver faster treatment for lung cancer patients. News Release. Calgary, Alberta: Alberta Health Services; 2011 16 December 2011.

2. BTS recommendations to respiratory physicians for organising the care of patients with lung cancer. the lung cancer working party of the british thoracic society standards of care committee. Thorax. 1998 Jun;53 Suppl 1:S1-8.

3. Alberts WM, Bepler G, Hazelton T, Ruckdeschel JC, Williams JH,Jr, American College of Chest Physicians. Lung cancer. practice organization. Chest. 2003 Jan;123(1 Suppl):332S-7S.

4. Jakobsen E, Green A, Oesterlind K, Rasmussen TR, Iachina M, Palshof T. Nationwide quality improvement in lung cancer care: The role of the danish lung cancer group and registry. J Thorac Oncol. 2013 Oct;8(10):1238-47.

5. Tucker TC, Howe HL, Weir HK. Certification for population-based cancer registries. J Reg Mgmt. 1999;26:24-27.

6. Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S, et al. The aarhus statement: Improving design and reporting of studies on early cancer diagnosis. Br J Cancer. 2012 Mar 27;106(7):1262-7.

7. Walter F, Webster A, Scott S, Emery J. The andersen model of total patient delay: A systematic review of its application in cancer diagnosis. J Health Serv Res Policy. 2012 Apr;17(2):110-8.

8. Gavrielov-Yusim N, Friger M. Use of administrative medical databases in population-based research. J Epidemiol Community Health. 2014 Mar;68(3):283-7.

9. Li X, Hilsden R, Hossain S, Fleming J, Winget M. Validation of administrative data sources for endoscopy utilization in colorectal cancer diagnosis. BMC Health Serv Res. 2012 Oct 13;12:358,6963-12-358.

10. Morgenstern H. Uses of ecologic analysis in epidemiologic research. Am J Public Health. 1982 Dec;72(12):1336-44.

11. Bardell T, Belliveau P, Kong W, Mackillop WJ. Waiting times for cancer surgery in ontario: 1984-2000. Clin Oncol (R Coll Radiol). 2006 Jun;18(5):401-9.

12. Simunovic M, Theriault ME, Paszat L, Coates A, Whelan T, Holowaty E, et al. Using administrative databases to measure waiting times for patients undergoing major cancer surgery in ontario, 1993-2000. Can J Surg. 2005 Apr;48(2):137-42.

13. Johnston GM, MacGarvie VL, Elliott D, Dewar RA, MacIntyre MM, Nolan MC. Radiotherapy wait times for patients with a diagnosis of invasive cancer, 1992-2000. Clin Invest Med. 2004 Jun;27(3):142-56.

14. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Impact of deprivation and rural residence on treatment of colorectal and lung cancer. Br J Cancer. 2002 Sep 9;87(6):585-90.

15. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American college of chest physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e142S-65S.