VARIATION IN WAITING TIMES FROM DIAGNOSIS TO TREATMENT FOR BREAST CANCER PATIENTS IN ALBERTA FROM 1997-2000

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BSc., University of Lethbridge, 2001

A Thesis
Submitted to the School of Graduate Studies
of the University of Lethbridge
in Partial Fulfillment of the
Requirements for the Degree

MASTER OF SCIENCE

Health Science
University of Lethbridge
LETHBRIDGE, ALBERTA, CANADA

ABSTRACT

There is considerable evidence that delays in diagnosing and treating breast cancer reduce long-term survival. The purpose of this study was to assess the waiting time between diagnosis and treatment for Alberta women with breast cancer and to examine the influence of age, cancer stage, Regional Health Authority (RHA), community size, and year of diagnosis on this time interval.

The data were obtained from the Alberta Cancer Board. The information included approximately all Alberta women with breast cancer between 1997 and 2000.

The overall median waiting time was 17 days. The mean and median delay increased by an average of two days each year. Only 43.8% of cases were treated within the recommended 14 days. The delay was significantly longer for women younger than 70, with stage 1 disease and from Northern RHAs. Efforts must be made to decrease delay and ensure that all women receive equal access to health services.

ACKNOWLEDGEMENTS

I would like to recognize all of those people who provided me with support, guidance and assistance in the development and completion of this research project. First, I would like to sincerely thank my supervisors, Dean Patricia Wall and Dr. Paul Hasselback. Despite being exceptionally busy, they both agreed to advise me and provided me with important insights and comments. Thank you also to Darlene for undertaking the difficult task of coordinating all of our schedules so that we could meet.

I would like to thank the Alberta Cancer Board for providing me with the data for this study.

I would like to extend a special thank you to Dr. Robert Williams, who helped me tremendously with the statistical methodology and the translation of the results.

I would also like to thank Dr. Karran Thorpe and, again, my supervisor Pat for inviting me to work with them in the evaluation of the Breast Health Program. This was an invaluable research and personal experience that allowed me to develop a better understanding of the human aspect of breast cancer rather than just the statistical side.

I would like to thank Nadine for taking the time to proofread my chapter drafts, for the very useful comments, helping me with formatting, and for continually supporting me.

Finally, I would like to thank those people that are most important to me. I thank my parents and grandparents for their constant support and belief in me. I

would like to thank all of my family and friends for their encouragement and prayers. A very special thank you to my husband who calmed me when I was stressed, understands and supports my education and career aspirations, and cooked and cleaned so that I could finish this thesis. Most importantly, I want to thank God for His endless blessings.

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CSSO……Canadian Society for Surgical Oncology

RHA……Regional Health Authority

CHAPTER 1: INTRODUCTION

Breast cancer is a disease with a significant impact on women's health. In most western countries, it continues to be the most commonly diagnosed cancer among women (excluding non-melanoma skin cancer) and the second leading cause of female cancer deaths (1). In Canada, 1 in 9 women are expected to be diagnosed with breast cancer and 1 in 26 women are expected to die from it (2). Breast cancer accounts for 31% of newly diagnosed cancers and 17% of cancer deaths in Canadian women (2).

The exact causes of breast cancer are not known. However, research has provided information regarding personal characteristics and factors that increase the risk of developing this disease. Combining all of these known risk factors still only accounts for approximately 30% of cases (2). The strongest risk factors include being 50 years of age or older, a carrier of the $BRCA_1$ or $BRCA_2$ gene, a strong family history of breast cancer, being born in Northern Europe or North America, and previously having breast cancer (2). Experiencing longer exposure to estrogen either through an early menarche (before 12 years) or a late menopause (after 50 years) and late childbearing (after 30 years) are other well documented factors that can impact the likelihood of developing breast cancer (2).

The majority of these risk factors are unavoidable and cannot be modified, making prevention difficult.

Because there is presently no primary prevention available for breast cancer, early detection and treatment are the best options for improving outcomes (3). The effect that delays in diagnosing and treating the disease have on survival remains controversial, as many studies have reported contradictory evidence. While some authors have found an improved survival rate for patients with shorter delays (4-15), other investigators have failed to find a difference (16-21), and one study has even reported better survival for patients with longer delays (22). However, research has tended to demonstrate that increased delay in the diagnosis and treatment of breast cancer can result in more advanced stages of the disease (3, 8, 11, 15, 23, 24). The stage (dependent on the size of tumor and whether it has spread) is widely recognized as the most important prognostic factor for breast cancer patients (15). Therefore, logically it should follow that delay can result in poorer chances for survival because of "stage drift" (15). This concept is based on the belief that tumors follow a time-dependent, linear progression through the different stages until metastasis occurs. The probability of successfully treating the disease decreases with later stage assessment (11, 15). There are many points in the process leading to treatment at which delay can occur and impact the outcome of the patient.

There is a common series of events that leads to the definitive treatment (the initial surgery or drug treatment) of breast cancer (Figure 1) (25). The first stage is detection of an abnormality, which can occur through self-examination,

examination by a health care professional, or a screening mammogram. After a health care provider confirms that there is a change in the breast tissue or a suspicious finding, the patient is often referred to a specialist who can perform a fine-needle aspiration, a needle biopsy or a surgical biopsy to provide a definitive diagnosis. After diagnosis, the patient must consult with a specialist regarding appropriate treatment, decide which treatment to receive and book the first treatment. It is obvious, then, that there are numerous points in the care pathway at which the patient could experience a delay. The literature often divides these points into two phases of delay: patient delay and system delay. Patient delay is defined as the time interval between the patient first noticing a breast cancer symptom and first medical consultation (3, 26). System delay is the time interval from when the patient first presents to a health care provider to treatment, which is sometimes further divided into the period from first contact with a family physician to specialist referral, from referral to treatment, or from diagnosis to treatment (3, 26).

Most studies examining the impact that delay has on survival and factors associated with increased waiting times have dealt with the patient delay interval. While studies have recently described baseline waiting time data for system delay, few studies have been conducted that look at factors that influence this waiting time (22, 27-32). The purpose of this study is to examine a portion of system delay and the factors associated with a prolonged delay during this time interval.

Specifically, this study is designed to assess variation in the waiting times for Alberta breast cancer patients from definitive diagnosis to definitive treatment.

Determining this variation is very important for planning appropriate health services and ensuring equal access to these services. Selected factors (age, stage, Regional Health Authority, Regional Health Authority category, community size, and year of diagnosis) that might affect access to and utilization of breast health services will be analyzed to determine relationship to and degree of influence on the waiting period. Developing a better understanding of the factors and their impact on waiting times could result in the reduction of delays in cancer treatment, thereby improving health outcomes and reducing psychological morbidity that is imparted by anxiety during the waiting period.

This thesis is divided into five chapters. Chapter Two provides a review of the literature, highlighting four areas of breast cancer research. First, it considers waiting times for various intervals in the care pathway. Secondly, the impact that delay has on survival of patients and the potential reasons for contradictory evidence are discussed. Finally, factors that are associated with a long patient and provider delay are presented.

Chapter Three describes the objective of this study and specific research questions to be answered. It then discusses the data source, the quality and reliability of the data and the variables of interest. Finally it outlines the statistical methods employed to achieve the purpose of the study.

Chapter Four presents the results of the analyses. It statistically describes the population and waiting time data for the period studied and for various subgroups. The regression model developed, the relative importance of predictors of waiting time and other significant findings are presented and discussed.

Chapter Five provides answers to the research questions and discusses relevant findings. Each variable examined is discussed and the results are compared to those indicated in the literature. The limitations and strengths of the study are also identified. Finally, conclusions and recommendations for future research are presented.

CHAPTER 2: A REVIEW OF THE LITERATURE

2.1 Overview

The literature reviewed for this study was obtained by various means, including computer-assisted searches using electronic databases (Medline, CINAHL, HKN, and CancerLit), the Internet, the Science Citation Index, and by consulting references used by relevant studies.

There were four primary areas of breast cancer research that were reviewed: 1) reports of baseline data for care pathway waiting times; 2) the impact that delay has on survival of patients; 3) factors that are associated with a long patient delay and; 4) factors associated with a long system delay. This chapter will examine, evaluate, and integrate studies pertinent to each of these areas.

2.2 Baseline Data on Waiting Times

Expert groups have attempted to set standards of maximum acceptable waiting times between key events in the care pathway for cancer treatment (33-36). The Canadian Society for Surgical Oncology (CSSO) has declared that no more than two weeks should transpire between the initial referral by a general

practitioner and consultation with a specialist or between diagnosis and initiation of treatment (33). The Canadian Association of Radiation Oncologists (CARO) has suggested that waiting for radiotherapy should not exceed 10 working days (34). The Canadian Strategy for Cancer Control (CSCC) set a four week goal for the interval between presentation of symptoms to a general practitioner and definitive diagnosis, while the National Health Service (NHS) in the United Kingdom (UK) set a two week goal for the period between referral and first outpatient appointment (35, 36). Furthermore, the NHS promised a maximum one month wait between diagnosis and treatment by 2001 and a maximum two month wait between urgent general practitioner referrals and treatment by 2002 for breast cancer patients (36). However, few recent studies have attempted to quantify actual waiting times for these key events.

Adam et al conducted a study that examined the waiting times for three intervals: i) first suspicion of an abnormality to first general practitioner consultation, ii) general practitioner consultation to first visit with a surgeon and iii) first surgical visit to definitive treatment (37). More than a two week period for each interval was defined as a delay. This study utilized a structured interview to elicit key dates and information from 162 women with breast cancer between 1978 and 1979 in London, England. They reported that 66 women (40.7%) were delayed at the first interval, 41 (25.3%) at the second interval and 57 (35.2%) at the third interval. Combining the data, 114 women (70.4%) experienced delay at some point before being treated for breast cancer. The authors concluded that

delay during the care pathway for breast cancer patients is a problem and needs attention.

In a similar study based on structured interviews, Colbert looked at the waiting times between the referral by a general practitioner and first visit with a surgeon (38). The sample consisted of 62 women who had breast cancer between 1991 and 1992 in North Wales or Wirral. The author found that only 21 women (34%) did not see a surgeon within two weeks of referral by a general practitioner and only 4 (6%) waited between six weeks and three months. Additionally, just 17 women (26%) waited more than four weeks for surgery after the initial surgical consultation. Of greater concern, however, were the findings that 4 women (6%) presented too late for surgery and 6 (10%) waited between three and nine months for a malignant diagnosis, which the author declared unacceptable.

The results reported by Adam et al and Colbert could have been biased by patient memory and the truthfulness with which the dates were reported. The dates given by the patients during the interviews may not have been exact, with no way to ensure the accuracy of the reports. Furthermore, the samples in both studies were small, leading to problems with generalizing the results to other situations. Generalizability was more problematic in the Colbert study because the same oncologist treated the patients. In order to limit the selective recall bias and provide a larger scope of waiting times, more recent studies have used cancer registries and large data bases to provide baseline waiting time data (22, 27-32) (Table1, Figure 2).

Table 1: A summary of studies that have reported baseline data for cancer care pathway waiting times.

Author	Year(s) Studied	Country	n	Interval(s) Studied	Median Waiting Period
Mackillop et al	1982-1991	Canada	4971	definitive diagnosis to radiotherapy	61 days
Caplan et al	1991-1995	USA	1659	i) clinical breast exam or mammogram to diagnosis ii) diagnosis to treatment initiation iii) abnormal screening result to treatment initiation	i) 32 days ii) 10 days iii) 48 days
Mayo et al	1992-1998	Canada	27515	first diagnostic procedure to surgical treatment	34 days
Olivotto et al	1996	Canada	13958	i) screening examination to first GP visit ii) screening examination to diagnosis	i) 18 days ii) 26 days
Sainsbury et al	1976-1995	UK	36222	i) referral by GP to first surgical visit ii) first specialist visit to definitive treatment	i) 10 days in 1976, 12 days in 1995 ii) 7 days in 1976, 13 days in 1995
Spurgeon et al	1997	UK	1517	i) referral by GP to first surgical visit ii) referral by GP to definitive treatment	i) 9 days and 14 days for urgent and non-urgent cases, respectively ii) 27 days and 35 days for urgent and non-urgent cases, respectively
Simunovic et al*	2000	Canada	440	i) referral by GP to first surgical visit ii) first surgical visit to treatment decision iii) treatment decision to initiation of treatment iv) referral by GP to initiation of treatment	i) 11 days ii) 0 days iii) 20 days iv) 37 days

*This study did not look solely at breast cancer.

In a study that examined the time between diagnosis and commencement of radiation therapy in Ontario, Mackillop and colleagues found that the median waiting time for 4971 women was 61.5 days (27). This study included seven Ontario cancer centres and considered the years from 1982 to 1991. The authors reported that over the course of the 10 years, the number of patients who were treated within the recommended four weeks from referral steadily decreased. More alarming was the finding that the wait between completion of surgery and beginning of postoperative radiotherapy increased by nearly 103%.

In a later Canadian study, Mayo et al also established that the wait for breast cancer treatment increased over time (29). This study looked at the number of days between the initiation of diagnostic procedures and surgical treatment for all women in Quebec with breast cancer between 1992 and 1998. For the entire time period, the median number of days for this interval was 34; however, it increased from 29 days in 1992 to 42 days in 1998.

Caplan et al looked at the intervals from clinical breast exam to diagnosis, diagnosis to treatment initiation and abnormal screening result to treatment (28). All women who were screen tested through the National Breast and Cervical Cancer Early Detection Program in the United States during the years 1991-1995 were included in this study. Median waiting times for the 1659 women were found to be 32 days, 10 days, and 48 days, for each interval respectively, suggesting that most women in this program received timely follow-up care after an abnormal screening examination.

A Canadian study that also looked at timeliness of follow-up after breast cancer screening for 15 342 women reported an even shorter median waiting period between screening examination and diagnosis than the American study (26 days versus 32 days) (30). Ten percent of the women had to wait 79 days or more for their diagnosis after an abnormal screening result.

Sainsbury et al evaluated the time elapsed from first visit to a general practitioner to first surgical visit and from first surgical visit to definitive treatment (22). This retrospective analysis of 36 222 breast cancer patients listed in the Yorkshire Cancer Registry between 1976 and 1995 indicated that the median delay from general practitioner referral to surgical visit had changed little over the years. On the other hand, median delay between surgical visit and treatment nearly doubled from seven days to 13 days during this same period of time.

Spurgeon and colleagues looked at the waiting times between general practitioner referral to first surgical visit and between referral to definitive treatment for cancer patients in England in 1997 (31). Of the 13 454 patients studied, 1517 were breast cancer patients. The authors separately analyzed urgent and non-urgent referral cases. They reported that the median times to first surgical visit were nine and 14 days for urgent and non-urgent referrals, respectively.

Simunovic et al also conducted a multi-cancer study examining the waiting periods from general practitioner referral to first surgical visit, first visit to treatment decision, treatment decision to treatment, and the total wait from

referral to treatment (32). The sample consisted of 1456 cancer patients in Ontario, with breast cancer being the most frequent diagnosis (n=440). The median times for the four intervals resulting from all of the cancer data were 11 days, 0 days, 20 days, and 37 days, respectively. The surgeons who participated in the study deemed that 37.2% of the patients had to wait too long for surgery. Considering the CSSO recommendation that treatment should be started no more than two weeks after diagnosis, the authors were concerned that the median time was found to be 20 days and that only 32.5% of the cases met this guideline.

Few of the studies reviewed reported baseline waiting times for the same intervals, making it difficult to compare them and to arrive at conclusions about the average time patients should expect to wait. Many of the authors expressed concern regarding the number of days some patients waited at various intervals in the care pathway. However, the following section demonstrates that there is no universal definition of what a delay is nor is there an agreement on the impact that delay has on prognosis.

2.3 Impact of Delay on Survival

Over the past 30 years numerous studies have examined the impact that patient and system delays have on the long-term survival of breast cancer patients (4-22). Controversy regarding this relationship is still prevalent because of the contradictory evidence reported by studies. The results from these studies can be divided into two categories: those reporting that extended delays reduce the

likelihood of long-term survival versus those reporting that lengthy delays do not impact long-term survival (Tables 2 and 3).

The conflicting results may be accounted for by several factors, including differences in sample characteristics (e.g. which stages of cancer are included or the age cut-off); differences in the delay interval studied (e.g. patient vs. provider delay); differences in the definition of delay (e.g. 3 months vs. 9 months); and the point from which survival time was measured (e.g. first symptom, diagnosis or treatment) (15). The summaries of the studies presented in Tables 2 and 3 demonstrate the array of methodological approaches. Given the differences in the studies, it is difficult to directly compare them; however, it is possible to evaluate them based on the aforementioned factors.

Richards and colleagues conducted a systematic review in 1999 of observational studies that examined the association between the duration of symptoms and survival for breast cancer patients (14). This meta-analysis consisted of 87 studies between the years of 1939 and 1996 with a total of 101 954 patients. The authors reported that the five-year survival rates (measured from date of diagnosis) were significantly lower for patients with longer patient delays ($p<0.05$). More specifically, those patients who delayed seeking help for three months or more had a 12% lower five-year survival than those with delays of less than three months and those with delays between three and six months had a 7% lower five-year survival rate. These results indicate that longer patient delay intervals are associated with lower survival rates.

Table 2: A summary of studies that indicate delay has a negative impact on the survival of breast cancer patients.

Author	Country	n	Sample Restrictions	Setting of Data Collection	Interval Studied	Definition Of Delay	Survival Measured From
Elwood and Moorehead	Canada	1545	None	Single site	First symptom to diagnosis	>12 months	First symptom
Feldman et al	USA	664	None	Multiple sites	First symptom to first visit	>3 months	Diagnosis
Charlson	USA	685	None	Single site	First symptom to treatment	>3 months	Treatment
Vernon	USA	1983	None	Single site	First symptom to first visit	>3 months	Diagnosis
Hainsworth et al	Australia	548	None	Single site	First symptom to first visit	>18 months	First symptom and diagnosis
Huguley et al	USA	2093	None	Multiple sites	First symptom to first visit; First visit to diagnosis; First symptom to diagnosis	>2 months	Diagnosis
Rossi et al	Italy	189	None	Single site	First symptom to treatment	>3 months	N/A
Rabinovich et al	Argentina	1067	None	Multiple sites	First symptom to treatment	>3 months	Treatment
Afzelius et al	Denmark	7608	None	Multiple sites	First symptom to first visit; First visit to definitive surgery or biopsy	>60 days	Treatment
Raabe et al	Norway	2704	None	Multiple sites	First symptom to treatment	>6 months	Diagnosis
Richards[2] et al	UK	2964	None	Single site	First symptom to first visit; First visit to treatment; Onset of symptoms to treatment	>12 weeks	First symptom and diagnosis
Richards et al	International	101954	None	Meta-analysis	Patient and Provider delay	>3-6 months	Diagnosis

Table 3: A summary of studies that indicate delay does not adversely affect survival of breast cancer patients.

Author	**Country**	**n**	**Sample Restrictions**	**Setting of Data Collection**	**Interval Studied**	**Definition of Delay**	**Survival Measured From**
Alderson et al	UK	258	Operable only*	Single site	First symptom to treatment	Continuous variable	Treatment
Dennis et al	USA	237	Operable only*	Single site	First symptom to first visit; First visit to treatment	>3 months	Treatment
Wallgren et al	Sweden	581	Operable only* <70 years	Single site	First symptom to first visit	>3 months	Treatment
Fisher et al	USA	1539	Operable only*	Multiple sites	First symptom to treatment	>9 months	Treatment
Neave et al	New Zealand	1675	None*	Population data	First symptom to diagnosis	>16 weeks	Diagnosis
Goodwin et al	USA	188	>65 years**	Population data	First symptom to first visit	>12 weeks	Diagnosis
Sainsbury et al	UK	5708	None**	Population data	Referral to treatment	>90 days	Family-physician referral

* Operable cancers are generally considered to be stage I and II.
** All stages of cancer are included.

The findings of Richards et al are consistent with earlier studies (4-13). Feldman et al, Vernon et al, Hainsworth et al, Huguley et al, and Afzelius et al all examined the patient delay interval (5, 7, 8, 9, 12). Feldman et al studied 664 patients with breast cancer in Brooklyn New York between 1975 and 1979 (5). The authors reported that patient delay was associated with poor survival for patients with aggressive (Class III) disease ($P<0.001$). In a study covering the same time frame as Feldman et al, Huguley and associates found that self-examiners were more likely to have a short patient delay and a higher five-year survival rate ($P<0.0001$) (9). In their study of 10-year survival rates for 1983 breast cancer patients, Vernon and colleagues reported that women with the least patient delay were more likely to survive ($P<0.001$) (7). An Australian study reported that patients who delayed presenting to their physician for 18 months or more had a significantly shorter five-year survival rate compared to those who presented earlier (42% versus 57%, $p=0.03$) (8). Afzelius et al determined that a short patient delay was associated with the longest survival ($p<0.0001$) (12). Patients who delayed presenting to a physician for more than 60 days had a 24% higher mortality rate than those who presented their symptoms earlier ($p<0.0001$).

Charlson, Rossi et al, Rabinovich et al, and Raabe and Fossaa studied the impact of total delay on survival and also found that long delays were associated with reduced likelihood of survival (6, 10, 11, 13). Charlson studied survival measured from treatment for 685 women with breast cancer at the Yale-New Haven Hospital between 1962 and 1969 (6). Patients with total delays of less than three months had significantly better survival rates than those with longer

delays ($p<0.001$). The study of 189 patients with primary breast cancer also indicated a significantly lower three-year survival rate for patients with a lengthy total delay ($p<0.05$) (10). A Norwegian study of 2704 patients separated total delay into three subgroups: short delay (<2 months, n= 1075); delay (>= 2 months and <6 months, n=643); and long delay (>= 6 months, n= 467) (13). The five-year survival rates for the three groups were 79%, 74% and 69%, respectively. The differences in survival rates between each group were significant ($p<0.05$). Similarly, Rabinovich et al divided total delay into three categories, but used three month intervals instead (11). Patients with a total delay of less than three months had statistically higher survival rates 10 years after treatment ($p=0.029$).

A major limitation of the meta-analysis and the other studies was that they did not control for lead-time bias. Lead-time bias arises when survival is measured from the date of diagnosis because the interval between diagnosis and survival will be shorter for those whose diagnosis was delayed, regardless of the association between delay and survival (14, 15, 26). Therefore, to overcome the effect of lead-time bias on survival data, length of survival should ideally be measured from the onset of symptoms (4, 15, 26). Richards et al were unable to present such an analysis because of missing data; however, Elwood and Moorehead and Richards[2] et al have conducted studies that did account for lead-time bias (4, 8, 15).

Elwood and Moorehead conducted a secondary data analysis that examined the influence of delay on survival for a population of 1545 breast cancer patients (4). They studied the interval from the first recorded symptom to

diagnosis and survival was measured from both the onset of symptom(s) and diagnosis. The authors reported that when survival was measured from the time of diagnosis, patients with a long delay (>12 months) had a 13% lower five-year survival rate than those with a shorter delay ($p<0.0001$) and when measured from onset of symptoms those with a long delay continued to show a significantly lower long-term survival ($p<0.001$). As a result, lead-time bias did not account for their conclusions and the results support the Richards et al finding that shorter delays do improve survival. Similarly, Richards[2] et al measured survival from both the date of diagnosis and the onset of symptoms (15). Delay was defined as the time from first symptom to first consultation with a medical professional. The data for the 2964 patients indicated that a long delay (>12 weeks) was associated with worse survival when survival was measured from both diagnosis ($p<0.001$) and onset of symptoms ($p<0.003$).

Although very few studies assess the impact of delay on survival from the onset of symptoms, the studies by Elwood and Moorehead and Richards[2] et al are important to consider (4, 8, 15). These studies provide evidence that lead-time bias may not be responsible for the long-term survival differences between long and short delay groups as noted by those studies that do not measure survival from symptom onset (5-7, 9-14). Others would argue that the results are sensitive to the patients' reports of onset of symptoms (26). The accuracy of the date of symptom onset cannot be verified and is influenced by the reliability of the patient's memory and the accuracy with which they report the date. If the date of

symptom onset is inaccurate, any subsequent analysis is subject to the bias (22, 26).

A second bias that may have influenced the results of the meta-analysis by Richards et al was their inability to include the study by Sainsbury and colleagues (22). Sainsbury et al conducted a population retrospective analysis of 36 222 breast cancer patients in the UK. This was the only study reviewed that measured survival from general practitioner referral and defined delay as the interval between referral and treatment (a component of provider delay). The authors found no evidence that long provider delays (>90 days) adversely impacted long-term survival. In fact, Sainsbury et al established that short provider delays (<30 days) were associated with poorer survival ($p<0.001$).

Correspondingly, in a study of 188 breast cancer patients older than 65 years of age, Goodwin et al found no adverse impact of patient delay on 10-year survival (21). In their evaluation of 549 breast cancer patients, Hainsworth et al found that patients who delayed seeking medical help for six months or more did not have a lower five-year survival rate compared to those who presented their symptoms to physicians within six months of discovery (8). Dennis and associates also examined the influence that patient delay has on survival and reported that delay did not predict survival (17). This study only included operable stage breast cancer patients, as did Alderson et al, Wallgren et al and Fisher et al (16, 18, 19). Two of these studies examined the interval from first symptom to treatment, while the other looked at time elapsed between first symptom and first medical consultation. These restricted sample studies all found

no significant relationship between delay and long-term survival. Although Feldman et al found that patients with aggressive disease who delayed were significantly less likely to survive, a separate analysis of patients with operable cancer did not support this relationship (5). A delay from symptom recognition to diagnosis was not found to influence survival by Neave et al in their study of 1675 breast cancer patients (20).

The phenotypic traits of the tumor could account for the contradictory evidence reported by Sainsbury et al and the other studies (26). Patients with phenotypically aggressive tumors may detect symptoms earlier and experience more severe symptoms causing them to seek medical advice earlier and physicians to react quicker (26). Because aggressive tumors would inherently predispose patients to worse outcomes, it would appear that those with short delays had a lower long-term survival (26). This is supported by Feldman et al's findings that survival was reduced by delay for patients with aggressive tumors, whereas this relationship did not hold true for patients with less aggressive disease (5). Further support is provided by the examination of survival for 160 women with breast cancer by Cummings et al (39). Results showed that the relationship between delay and long-term survival depended on the rate of tumor growth: patients with slow growing tumors who delayed had a shorter survival time, whereas the survival of patients with fast growing tumors was not affected by delay. Coates suggests that the impact of this bias is different for patient and provider delay (26). Afzelius et al supported this suggestion by reporting that longer provider delays were associated with improved outcomes, whereas longer

patient delays were associated with poorer outcomes (12). Therefore, it is possible to attribute the reduced survival with decreased provider delay, reported by Sainsbury and colleagues, to samples with more aggressive phenotypic traits and the ability of physicians to discern urgent cases and refer them faster.

With the exception of the Sainsbury et al study, the studies that reported that long delays do not negatively impact survival could be criticized on the basis of their sample inclusion criteria (16-21). These studies all included sample restrictions, whereas those studies that reported that delay lowers long-term survival had no sample restrictions (Tables 2 and 3). Alderson et al, Dennis et al, Wallgren et al, and Fisher et al restricted their samples to those patients with operable breast cancer only (generally stage I and II cancers) (16-19). Several studies have reported that within individual stages, longer delays have no adverse impact on survival, but when all stages are considered together delay does influence survival (4, 11, 15). Therefore, restricting the sample to stages I and II could reduce the chance that a survival difference would be observed.

In conclusion, those studies that have reported a negative association between delay and survival are, as a whole, more numerous and based on broader sample inclusion criteria. The results from these studies suggest that it is important to monitor waiting times at all intervals of the care pathway to ensure that patients' prognosis is not affected by long delays. Reduction of waiting times is one of the few means presently available in the fight against breast cancer mortality. Awareness of factors that contribute to delays could help prevent

unnecessary delays and the possible negative impact on survival. The following section will examine determinants of patient delay.

2.4 Factors Associated With Patient Delay

Delay by the patient is the interval from first symptom recognition to first medical consultation. Several studies have examined what causes patients to delay in presenting breast symptoms to a physician. Commonly studied variables include age, breast symptom and socioeconomic status, whereas education, ethnic origin, marital status, and family history have been studied to a lesser extent (Table 4).

Two problems arise when studying this component of delay. First, most studies obtain information and dates by interviewing the patients after a new diagnosis of cancer. The reliability and validity of the data are subject to recall bias of symptom recognition and the tendency to underreport the length of delay (40). It would follow then, that there is likely more patient delay than what is reported in the literature (40). Secondly, patient delay and provider delay are not mutually exclusive. The total time elapsed from symptom recognition to consultation might be increased if the patient has difficulty obtaining an appointment, which is attributable to the provider (3). However, the separate assessment of such cases is extremely difficult.

Table 4: A summary of studies that support or refute factors that are predictive of long patient delay.

Predictive Factor	**Supporting Studies**		**Refuting Studies**	
Age	Antonovsky and Hartman*	Arndt et al (n=287)	Adam et al (n=162)	Burgess et al (n=185)
	Afzelius et al (n=7608)	Coates et al (n=1470)	GIVIO (n=1110)	
	Hainsworth et al (n= 548)	Nichols et al (n=582)	Gould-Martin et al (n=274)	Menon et al (n=359)
	Ramirez et al*	Richards[2] et al (n=2964)	Mor et al (n=214)	Rossi et al (n=189)
	Richardson et al (n=28 486)			
	Schottenfield and Robbins (n=7000+)			
Absence of a breast lump	Burgess et al (n=185)	Coates et al (n=735)	Adam et al (n=162)	Arndt et al (n=287)
	Feldman et al (n=622)	Gould-Martin et al (n=274)	Mor et al (n=214)	Rossi et al (n=189)
	MacArthur and Smith (n=145)	Nichols et al (n=582)		
Low Socioeconomic Status	Antonovsky and Hartman*	Coates et al (n=735)	Burgess et al (n=185)	Mor et al (n=214)
	Gould-Martin et al (n=274)	Richardson et al (n=28 486)	Ramirez et al*	
	Samet et al (n=780)			
Less Education	Antonovsky and Hartman*	Coates et al (n=735)	Arndt et al (n=287)	Mor et al (n=214)
	Ramirez et al*		Samet et al (n=780)	
Non-White Ethnic Origin	Coates et al (n=735)	Ramirez et al*	Samet et al (n=780)	Dennis et al (n=237)
	Richardson et al (n=28 486)	Vernon et al (n=1983)		
Unmarried			Arndt et al (n=287)	Burgess et al (n=185)
			Mor et al (n=214)	Neal et al (n=810)
			Ramirez et al*	
			Richards[2] et al (n=2964)	
No Family Personal History of Breast Disease	Arndt et al (n=287)		Burgess et al (n=185)	
			Gould-Martin et al (n=274)	Samet et al (n=780)

*Literature Review

2.4.1 Age

The most commonly studied variable for impact on patient delay is age. In a systematic review of the literature that looked at risk factors predicting patient delay, Ramirez et al included 19 papers in their assessment (41). The authors concluded that the strongest determinant of patient delay was older age. That is, older patients waited longer to present their symptoms to a physician. Antonovsky and Hartman performed a review of the literature prior to 1974, and also reported that older age was commonly associated with a longer patient delay (40). A recent German study reaffirmed the strong association between older age and longer patient delay (P=0.01) (42). Patients over the age of 50 were three times as likely to delay seeking medical care for three months or more compared to women under 50 (24.7% versus 7.1%). Hainsworth et al also reported that delay (defined as more than six months) was associated with older age (median of 68 versus 65 years, p=0.042) (8). In a large London study of 2964 patients between 1975 and 1990, Richards[2] et al determined that patients older than 65 years had longer symptom duration (P<0.0001) (15). Similarly, in their study of new breast cancer patients, Nichols et al reported that women over 65 had an increased patient delay as well as more malignancies (43). The increased frequency of malignancies in this age group led the authors to speculate that age and diagnosis might not separately influence patient delay. Schottenfield and Robbins studied more than 7000 breast cancer patients during two separate time periods, 1949-55 and 1956-62 (44). They found that older women (>65 years) in both periods were more likely to delay in seeking medical care. During 1949-55

54% of women under 65 years were seen within three months of first symptom recognition, whereas only 48% of those older than 65 years were. During 1956-62, 58% of younger women versus 52% of older women were seen within three months. Afzelius and colleagues performed a study on patients with primary breast cancer who were registered in the Danish Breast Cancer Cooperative Group treatment programs between August 1977 and November 1982 (12). The results from the 7608 patients studied indicated that younger (<40 years) patients presented their symptoms to a physician significantly sooner than did older patients (>40 years). The median duration between first symptom recognition and first consultation with a physician was 10 days for younger women compared to 20 days for older women ($p<0.0001$).

Two studies have found the reverse relationship between age and patient delay. Richardson and associates examined the association between age and patient delay for 28 486 women with breast cancer in Los Angeles County between 1977 and 1985 (24). The authors found that older patients presented their symptoms to a physician sooner than younger women did (trend $P<0.001$). In their study of 1470 newly diagnosed breast cancer patients, Coates and colleagues established that younger women (<40 years) were more likely to delay consultation ($p<0.01$) (45).

Several studies have failed to find an association between age and patient delay. Burgess et al studied 185 women with breast cancer from the United Kingdom between 1992 and 1994 (46). They reported that age was not significantly associated with extent of patient delay ($P=0.1$). In their examination

of 1110 newly diagnosed breast cancer patients from 63 Italian hospitals, GIVIO indicated that no difference in patient delay was found between ages (23). Adam and colleagues performed a study with 162 women with breast cancer (37). Again, age was not found to influence patient delay. Gould-Martin et al examined 274 women in the Los Angeles County between 1967 and 1977 (47). The authors defined delay by a patient as greater than two weeks from detection of a symptom to presentation to a physician. No association between this delay and age of patient was found. In their assessment of 189 women in Rome, Rossi et al did not find that age influenced patient delay (10). Similarly, in the study of 359 Asian women performed by Menon et al, age was not found to be a determinant of patient delay (48). Although 16.5% of older patients (>35 years) compared to only 6.5% of younger women (≤35 years) waited more than a year to present their symptoms, no significant association was found. Mor et al divided their sample of 214 breast cancer patients into those younger than 45 years and 45 years and older (49). They reported that age was not a predictor of delay. Samet and associates studied 780 patients with newly diagnosed cancer, including those with cancer of the breast (50). Age was not found to influence patient delay; however, this sample only consisted of patients older than 65 years. In previously mentioned studies by Richards[2] et al and Nichols et al that did find an association between patient delay and age, it was women over the age of 65 who delayed significantly more (15, 43). Therefore the exclusion of patients under the age of 65 could account for lack of association found by Samet et al.

Close examination of Table 4 reveals a pattern in the number of individuals in the studies (n) that did and did not support the idea that age influences patient delay. Those studies where age was reported to be a predictive factor generally had larger sample sizes than studies that did not find an association. Only two studies that did report a difference in waiting times were based on samples of less than 1000 patients, whereas only one study that did not report a difference was based on a sample of this size or larger. The small samples of the studies could account for their inability to find an association between age and patient delay. This is due to the direct relationship between sample size and power of the statistical analysis. Power is a measure of the sensitivity of the analysis to detect an effect of the independent variable (i.e., an effect of age on patient delay) (51). The larger the power of the experiment the more likely an effect will be reported. Therefore, studies with larger sample sizes have a greater power to determine an association between age and patient delay. On the other hand, it is easy to find a statistically significant difference with large sample sizes even if the difference is not large enough to be clinically useful. It is important in these cases to also examine the clinical significance of the statistically significant results because the size of the difference may not be large enough to justify a change in clinical practice.

2.4.2 Breast Symptom

The influence that the symptom(s) discovered by women has on patient delay has also been evaluated by several studies. In a study of 162 women with

breast cancer, 70.4% of the women indicated that their presenting symptom was a painless lump, while 29.6% reported other symptoms, including a painful lump, breast pain and changed appearance of the breast (37). Although the authors indicated that symptoms other than a lump did lead to increased patient delay, the impact was not statistically significant. Arndt et al evaluated 287 women with newly diagnosed breast cancer and reported that patients who noticed a lump had somewhat shorter delays, but again this relationship was not significant (P=0.24) (42). Rossi and associates also reported that symptom at presentation was not a determinant of patient delay for their sample of 189 breast cancer patients (10). Although Mor et al found that patients who reported a lump were significantly more likely to think that they had breast cancer ($p<0.05$), they were not less likely to delay presenting their symptom to a physician (49).

While these studies reported no association, other studies have found the presenting symptom to be a significant predictor of patient delay. MacArthur and Smith studied 145 women with breast cancer from four hospitals in the UK (52). They divided initial symptom recognized by the women into three categories: a lump on its own; a lump together with another symptom(s); or another symptom without a lump. Those women who had a lump or a lump and another symptom were found to have similar delay patterns (median of 28.5 days versus 26 days, respectively). Therefore, the authors grouped the women with a lump together for the analysis of symptom impact on patient delay. Women who did not initially discover a lump were significantly more likely to delay in consulting a physician than those who had found a lump ($p=0.0262$). Of the 35 women who did not

initially discover a lump, 11 noticed one later. These women were separately analyzed from those who never found a lump and were found to have significantly different delay times (median of 56 days versus 86 days, respectively). MacArthur and Smith concluded that it is the absence of a lump, rather than the presence of another symptom that is important in predicting delay. They speculated that this difference in waiting times is the result of the focus of breast health public education on the classical symptom of the painless lump. In their study of 622 breast cancer cases, Feldman et al found that patients with symptoms other than a breast lump had significantly longer patient delay periods ($P<0.01$) (5). Burgess et al found that women with no breast lump were four times more likely to delay seeking medical attention for 12 weeks or more than those who had a lump (41% versus 10% of sample, respectively, $P<0.0001$) (46). Nichols and associates reported that in women older than 65 years, patient delay was associated with symptoms other than a lump, but the sample was too small to compare statistically (43). Coates et al reported that the absence of a lump was a significant determinant of patient delay for their sample of 735 women ($P<0.04$) (45). In their assessment of patient delay for 274 women, Gould-Martin and colleagues found that the most significant factor influencing delay was the type of initial symptom (47). Those women with a lump consulted a physician within a median of seven days, whereas those without a lump waited a median of 31 days ($P<0.001$).

2.4.3 Socioeconomic Status

A third common variable which has been studied regarding its impact on patient delay is socioeconomic status (SES). In their systematic review of 19 papers, Ramirez et al found that there was insufficient evidence to support their hypothesis that a lower SES led to increased delay by patients (41). Burgess et al studied 185 women who attended a breast unit in London (46). The authors found that SES was not significantly associated with patient delay (P=0.3). In their study of 214 newly diagnosed breast cancer patients from nine Rhode Island hospitals between 1984 and 1986, Mor et al reported that SES was not a predictor of delay (49).

When no association between the independent variable (SES) and the dependent variable (patient delay) is reported, it is important to consider the statistical power of the study. The small samples utilized by Burgess et al and Mor et al reduce the power to detect an effect of SES on patient delay and could account for their failure to determine SES as a predictive factor of delay (51). Those studies that did find an association between age and patient delay were based on larger samples, providing more power to their analyses (Table 4).

Antonovsky and Hartman concluded from their literature review that low SES was commonly associated with patients who delayed (40). In their assessments of the influence of SES on patient delay, Richardson et al and Coates et al both reported that delay increased with decreasing SES (trend P<0.001 and trend P<0.04, respectively) (24, 45). Gould-Martin et al found that patients with a

high SES had a median delay of 7 days, while those with a low SES had a median delay of 14 days (P<0.1) (47).

Samet et al did not specifically examine SES (50). However, they did look at the impact of income- a variable used in determining SES- on patient delay. They reported that mean annual income declined with increasing breast cancer patient delay (p<0.05).

2.4.4 Education

Although education can be used in SES classification, several studies have looked independently at the association between education and patient delay. Ramirez and colleagues indicated that there was moderate evidence from their systematic review of the literature that fewer years of education was associated with an increased patient delay (41). The literature review performed by Antonovsky and Hartman yielded the same conclusion that less education is a determinant of delay for breast cancer patients (40). Coates et al reported from their study of 735 women that those with more education waited less to present their symptoms (trend P<0.04) (45). However, three studies failed to determine that education was associated with patient delay (42, 49, 50).

2.4.5 Ethnic Origin

Given the discrepancy in breast cancer survival between white and non-white women, several studies have examined the impact of race on patient delay in an attempt to explain the prognosis difference. Ramirez et al hypothesized that

being of non-white origin was a predictor of patient delay (41). Their literature review offered what the authors deemed to be moderate evidence for this hypothesis. Richardson and colleagues studied 23 567 non-Hispanic Whites, 2539 Blacks and 2380 Hispanics from the Los Angeles County (24). Both the Hispanic and the Blacks were at greater risk of long patient delay compared to non-Hispanic Whites ($P<0.001$ and $P<0.001$, respectively). In the study of 1983 women from Texas, Vernon et al also divided their sample into White, Black and Hispanic women (7). Whites were more likely to see a physician within two months of noticing symptoms than were non-Whites ($P<0.001$). This difference was more pronounced between White and Black women than it was for White and Hispanic women. Coates et al, Samet et al and Dennis et al only divided their samples into two race categories (45, 50, 17). Coates and associates reviewed 410 Black and 325 White women (45). The authors found the median symptom duration was longer for Black women than for White women, bordering on significance (16 days versus 14 days, $P=0.06$). Samet et al reported that the difference in waiting time for Hispanics and non-Hispanics was not statistically significant (50). Dennis et al found no correlation between race (White or Black) and patient delay for 237 breast cancer patients (17). The small sample used by Burgess et al and the reduced power of the analysis could account for the reported lack of association between race and delay (51).

2.4.6 Marital Status

The marital status of women has also been examined for its influence on the patient delay interval. Prior to their literature review, Ramirez and colleagues hypothesized that being unmarried would increase the patient delay period (41). All articles included in the review regarding this association refuted their hypothesis. In their study of 287 women with breast cancer in Germany, Arndt et al failed to find a relationship between marital status and patient delay (P=0.13) (42). Neale et al studied 810 married and 320 widowed white women with breast cancer (53). The authors reported that 56.1% of married women and 55.6% of widowed women visited a physician within three months of symptom detection, resulting in a non-significant relationship between marital status and patient delay. Richards[2] et al's study was based on a sample of 2964 patients, 81.1% of which were married (15). No association between marital status and duration of patient delay was established. Burgess et al and Mor et al also failed to uncover an association between marital status and patient delay (46, 49).

2.4.7 Family History and Previous Breast Disease

One might speculate that women who have a family history of breast cancer or who had benign breast health problems themselves might be more aware of the problem and present to their physicians sooner than women with no past experience with breast disease. However, most of the studies that have examined this association have found no evidence to support this speculation. Burgess et al examined the impact of previous experience with cancer in family or

friends on the patient delay period, but found no significant difference between those with a history and those without one (P=0.8) (46). Samet and colleagues also found that a family history of cancer was not associated with decreased patient delay (50). Gould-Martin et al separately examined the impact of family history and a history of benign breast disease on patient delay (47). The authors reported that family history was not predictive of delay; however, they did find that women with past benign breast disease waited longer to consult a physician (P<0.1). An examination of breast cancer patients in Germany found an association between women with previous benign disease and long patient delay, but no relationship between family history and delay was identified (42). The authors suggested that patients with a previous benign breast disease waited longer to present to a physician because they attributed the new symptoms to their benign breast disease. Burgess et al reported that four of the 66 women (6%) who delayed consulting a physician indicated that they delayed because they attributed their symptom(s) to previous benign breast disease (46).

Numerous factors that could impact patient delay have been reviewed, including age, presenting symptom, socioeconomic status, education, ethnic origin, marital status, and past experience with a breast disease. Age has been the most commonly studied variable. There is considerable evidence that younger patients are less inclined to wait to present their symptoms to a physician. Most studies that did not support this connection had reduced power to demonstrate an association because of the small samples the studies were based on. The

existence of a lump as a presenting symptom also seems to reduce the patient delay interval. This could be accounted for by women's increased awareness of a lump as a breast cancer symptom because of public health education campaigns focusing on breast-self examinations for early lump discovery. The idea that patients of low SES experience more delay was substantiated by most of the studies examining this factor. Factors related to SES that were independently studied were education and ethnic origin. Being non-White seemed to increase the patient delay interval; however, education was not found to be associated with delay. The few studies that looked at marital status and family or personal history of breast cancer did not provide support that delay is impacted by these factors. Determinants of system delay have been studied much less extensively than those of patient delay. These factors are reviewed in the following section.

2.5 Factors Associated With System Delay

System delay is the interval from first medical consultation to treatment. Unlike patient delay, the system component is often further subdivided into the period from first consultation to referral to a specialist, the period from referral to treatment, and even smaller intervals of delay (26). Variables that could impact provider delay that have been examined include: age, breast symptom, diagnosis, ethnic origin, administrative problems, family history, and region (Table 5). Aside from these variables, increased delay might be attributable to the patient if she cancels or misses an appointment or chooses a later one. It is difficult to

Table 5: A summary of studies that support or refute factors that are predictive of long provider delay.

Predictive Factor	**Supporting Studies**		**Refuting Studies**
Age	Afzelius et al (n=7609) Caplan et al (n=1659) Finley and Francis (n=454) Sainsbury et al (n=18 846)	Burgess et al (n=185) Caplan et al (n=996) Ramirez et al*	Adam et al (n=162) Dennis et al (n=237)
Absence of a breast lump	Adam et al (n=162) Caplan et al (n=1659) Ramirez et al*	Burgess et al (n=185) Caplan et al (n=996)	Adam et al (n=162) MacArthur and Smith (n=145)
Diagnosis	Bywaters (n=180) Nichols et al (n=582)	Greer (n=157) Olivotto et al (n=13 958)	
Ethnic Origin/Race	Caplan et al (n=1659)	Dennis et al (n=237)	Caplan[2] et al (n=996) Ramirez et al*
Administrative Problems	Adam et al (n=162)		
No Family or Personal History of Breast Disease	Finley and Francis (n=454)		Adam et al (n=162)
Region	Caplan et al (n=1659) Mackillop et al (n=18 077) Spurgeon et al (n=1517)	Caplan et al (n=996) Olivotto et al (n=13 958)	

*Literature Review

determine cases when this occurs and completely separate and analyze delay attributable only to the system.

2.5.1 Age

Age is the most frequently examined factor of system delay. Two arguments can be made regarding the impact that age has on delay. First, it is possible that older patients will experience more provider delay because physicians will not feel it necessary to quickly treat them based on their longevity. On the other hand, younger women might be delayed more because physicians will regard them as low risk for breast cancer. The latter association has been reported by several studies.

The systematic review conducted by Ramirez et al yielded strong evidence for their hypothesis that younger age is a risk factor for provider delay (41). They found that four of the five articles reported this association between age and provider delay, consisting of a total sample of 5146 patients, whereas the non-supporting paper had a sample of 200 patients. Caplan[2] and colleagues studied the interval between diagnosis and treatment for 996 breast cancer patients between 1985 and 1986 (54). The authors reported that younger age was significantly associated with longer treatment intervals (trend $p<0.001$). This association countered their hypothesis that older women would experience more delay because the system would not feel obliged to evaluate and treat older women aggressively. In a later study by Caplan et al, younger age (<70 years) was also found to be predictive of treatment delay ($p=0.035$) for the 1659 women

studied (28). Burgess and colleagues examined general practitioner delay for 185 women with breast cancer (46). General practitioner delay was defined as the interval from first contact with a physician to subsequent referral to a specialist. Again, compared to older patients, younger patients were more likely to experience delay (mean of 55 versus 49 days, respectively, P=0.01). Finley and Francis and Afzelius et al also looked at the influence of age on physician delay, but defined this period as the time between first contact and biopsy or treatment, rather than referral (55, 12). Both studies reported significant trends in the negative association between age and physician delay ($p=0.03$ and $p<0.0001$). In their study, Sainsbury et al examined the interval from referral to treatment for 18 846 patients with breast cancer (22). Overall, 48% (2061) of those patients younger than 50 years received their treatment within 30 days of family-physician referral, compared with 64% (9313) of patients older than 50 years ($p<0.001$). Furthermore, 90 days after referral, 8% of younger patients compared to 3% of older women still had not been referred ($p<0.001$). The authors concluded that this negative relationship between age and system delay was due to physicians being more suspicious of breast cancer in older women and referring them to a specialist faster.

Two studies did not confirm that younger age predicted system delay (17, 32). One of these studies evaluated the waiting times for the intervals from referral to first visit to a surgeon, first surgical visit to treatment decision and from treatment decision to surgery for eight regional cancer centres in Ontario (32). The duration of each interval was not significantly impacted by patient age.

2.5.2 Breast Symptom

The breast symptom that the patient presents to a physician might impact system delay. The hypothesis that presenting to a physician with a symptom other than a lump is predictive of system delay was strongly supported by all of the pertinent articles reviewed by Ramirez et al (total of 1476 patients) (41). In a study of 185 women with breast cancer, referral delay by the general practitioner was significantly associated with symptoms other than a lump (P=0.002) (46). The women who presented with no lump were three times more likely to be delayed than those who had a lump. Adam et al examined the interval from first contact with a general practitioner to outpatient appointment for 162 women with newly diagnosed breast cancer (37). The failure of the general practitioner to attribute the symptom to breast cancer was the most common reason for delay, occurring in 46.3% of the sample. Caplan[2] and associates determined that for White and Black women, the presence of a lump was associated with shorter system delay (defined as interval from first physician contact to definitive diagnosis) compared to other symptoms; however, symptomatic women tended to have shorter system delays than asymptomatic women (mean of 10.7 days versus 89.3 days) (54). The authors attributed the noted relationship between a shorter system delay and presence of a lump to the commonality of the painless lump as a recognized breast cancer symptom by physicians, which expedites their response. A later study by Caplan et al also indicated that women with breast cancer

symptoms had a significantly shorter delay interval from abnormal mammogram to treatment than those with no symptoms (p=0.013) (28).

MacArthur and Smith independently looked at two phases of system delay: from first medical contact to referral for specialist opinion; and from referral to definitive treatment (52). Within two days of first visit, 89.5% of patients with a lump and 85.5% with a lump and other symptom were referred compared to only 42% of those without a lump (p=0.0001). However, delay from referral to treatment was not significantly affected by the symptom. Adam et al found no significant association between length of various system delay intervals and different symptoms (37).

2.5.3 Diagnosis

One might expect that patients with malignant disease of the breast to experience shorter system delays than those with benign breast diseases. Few studies have looked at this association. In a recent study of seven provincial screening programs, Olivotto et al reported that women found to have breast cancer had shorter times to diagnosis than did women whose biopsy indicated benign disease (30). Nichols et al studied doctor delay (interval from first physician consultation to referral to surgical unit) and hospital delay (referral to outpatient attendance at surgical unit) (43). Both of these intervals were significantly reduced in malignant cases. The median length of doctor delay was one day for malignant cases and four days for benign cases (P<0.10). The median hospital delay was nine days for malignant cases and 13 days for benign cases

(P<0.005). The authors concluded that physicians were generally able to distinguish between malignant and benign breast disease at first contact. Bywaters noted that on average patients with breast cancer had a biopsy four times as fast as those with benign conditions (10.1 days versus 40.9 days) (56). Greer found that 19% of malignant cases compared to 24 % of benign cases were delayed more than five weeks from first consultation to biopsy (57). This result was not significant.

2.5.4 Ethnic Origin/Race

Few studies have assessed the impact of ethnicity on system delay. Ramirez et al hypothesized that being of non-White ethnic origin would increase system delay (41). However, their review of the literature provided moderate evidence against this hypothesis. Caplan[2] et al's study of 477 White and 519 Black patients with breast cancer also yielded no relationship between race and system delay (54).

While these studies indicated that ethnic origin is not a determinant of system delay, two other studies have found a relationship. Caplan and colleagues studied the diagnostic interval (time from abnormal screening to diagnosis), treatment interval (time from diagnosis to treatment initiation) and total delay interval (time from abnormal screening to treatment initiation) (28). The sample consisted of 1659 women of various ethnic origins, including white (n=975), Black (n=255), Hispanic (n=270), Asian (n=45), American Indian/Alaskan Native (n=97), and other/unknown (n=17), who were part of the National Breast and

Cervical Cancer Early Detection Program (NBCCEDP) between 1991 and 1995. Compared to all other races, white patients had significantly shorter diagnostic delay (median of 29 days versus 34.2 days, respectively, P<0.0001). Significantly shorter treatment and total delay was also experienced by white patients compared to all other race and ethnic groups (P<0.004, P<0.0001, respectively). Dennis et al reported that the interval from first medical consultation to treatment was greater for Black patients, however, no significance values were reported (17).

2.5.5 Administrative Problems

Administrative problems include factors that contribute to delay that are not attributable in any way to the patient or her characteristics, including appointments, beds, rescheduling because of physician absence and missed diagnoses. Delay between general practitioner and outpatient appointment and between outpatient appointment and definitive treatment for 162 patients was examined by Adam et al (37). The second most common reason for delay in receiving a surgical visit was a problem in obtaining an appointment. This difficulty occurred for 36.6% of patients. Delay in treatment was most commonly the result of other administrative problems, including waiting for a hospital bed, the inability of the physician to offer a definitive diagnosis and the selection of treatment.

2.5.6 Family History and Previous Breast Disease

A patient with a personal or family history of breast problems could be perceived as high risk by providers and experience less delay. In a study of 454 breast cancer patients in the United States, Finley and Francis examined factors associated with physician delay (55). This interval was considered the time elapsed from first contact with a physician to a biopsy and a delay was defined as more than 30 days for this period. A family history of breast cancer was positively associated with physician delay (p=0.03), however, a personal history of breast cancer was not. Adam et al reported that no component of system delay was influenced by whether or not the woman had a positive family history of breast cancer (37).

2.5.7 Region

Centralization of specialty services could impact the waiting times of patients who live far and close to the treatment centre. Spurgeon et al examined waiting times for cancer patients in England after a referral from a general practitioner to first surgical visit and definitive treatment (31). Breast cancer was the most frequent type of cancer in the sample (n=1517). The authors indicated that there was significant variation in patients' waiting times according to where the treatment was provided. Two American studies have also shown that regional variation exists in the system delay waiting period (28, 54). One of these studies also showed that delay was shorter for rural than for urban women (p=0.002) (28). The time to receive a diagnosis after an abnormal screening examination for

13 958 women across screening programs in Canada was shown to vary considerably between programs (30). Mackillop et al studied the interval between diagnosis and initiation of radiation treatment for all patients receiving primary radiotherapy for carcinoma of the larynx, cervix, lung, and prostate at seven Ontario cancer centers between 1982 and 1991 (27). The authors reported significant intercentre variations in median waiting times. A third Canadian study based on a sample of 1456 cancer patients from eight regional cancer centres in Ontario examined several delay intervals, including time from general practitioner referral to treatment (32). Patients included in the study were being treated for breast, gynecologic, colorectal, head and neck, thoracic, or urologic cancers. Median number of days from referral to treatment varied substantially across cancer centres (range of a median 19.0 days to 43.0 days). These studies provide evidence that equal access and care may not be provided by different centres.

Although determinants of provider delay have been studied less than those of patient delay, some general conclusions can still be drawn. First, the idea that younger women experience more provider delay was substantiated by most of the studies. This is the opposite of the relationship found for patient delay. It seems that providers do not anticipate younger women to have breast cancer because they are at lower risk and, as a result, do not treat them as expediently as older women who are inherently at greater risk for the disease. Secondly, there is moderate evidence that women who present to a physician without a lump wait longer. Again, this could be because a lump is recognized as a very common

indication of breast cancer leading the physicians to act more promptly. Thirdly, women who had malignant breast disease were pushed through the system quicker than women with benign disease. The last important conclusion that can be made is that the region that the patient is treated in (ie., the hospital) or lives in (rural versus urban) affects the waiting time. Very few studies examined the impact of ethnic origin, administrative problems and previous experience with breast disease on provider delay.

2.6 Summary

This chapter provided a review of the literature with reference to baseline waiting times for breast cancer patients at various intervals in the care pathway, the impact that delay has on prognosis and factors associated with patient and provider delay. Early studies interviewed patients to determine median waiting times, whereas subsequent studies have used cancer registries and databases for this purpose. Median waiting times for numerous intervals in the care pathway have been reported. Two alarming findings by recent Canadian studies were that waiting times have been increasing over time and that an unacceptably small fraction of women were treated within the recommended time (29, 30). Determining baseline waiting times for intervals in the care pathway leading to breast cancer treatment continues to be important for providers assessing the appropriateness of waiting times experienced by patients.

The impact that delay in the care pathway has on the long-term survival of patients is controversial because of the contradictory evidence reported by studies. Problems and biases of the studies were discussed in an attempt to explain the conflicting results of those studies that reported delay reduced survival and those that did not discover this association. There is evidence that long delays by the patient and the provider result in worse outcomes.

Finally, variables that could impact patient and provider delay were examined in detail, including age, presenting symptom, socioeconomic status, ethnic origin, region and other less studied factors. More studies have focused on determining factors associated with patient delay than provider delay. Given the evidence that long provider delays can reduce long-term survival, more research needs to be done to further substantiate predictors of provider delay. Further knowledge of determinants of delay could allow providers to identify patients at high risk of experiencing long waits and to design interventions to minimize delay.

The following chapter will briefly describe the rationale for this study based on the review of the literature presented in this chapter. It will then outline the research questions and the hypotheses for each question. The data source and quality will also be discussed. Finally, the variables and statistical methods employed to answer the questions will be described.

CHAPTER 3: STUDY DESIGN AND METHODOLOGY

3.1 Introduction

The previous chapter provided a review of the literature concerning baseline waiting times, the impact of delay on survival and factors associated with long patient and provider delays. Given that long provider delay was shown to be associated with reduced survival and that it has been less studied than patient delay, it was noted that more research needs to focus on the provider delay period. Coates and associates have indicated that it is important to independently examine factors associated with the different subdivisions of provider delay (i.e., from first presentation to a general practitioner to specialist referral, first visit with specialist to diagnosis, and from diagnosis to initiation of treatment) because different interventions to minimize delay could exist for each period (45). Based on these findings, this study specifically examined the interval from diagnosis to treatment for all women with breast cancer in Alberta in the years of 1997-2000.

This chapter will outline the research questions and the quantitative methods used to answer these questions. It will examine the registry the data were obtained from, the study population, the study variables, and the statistical methods employed.

3.2 Research Questions and Hypotheses

The objective of this study was to identify predictors of delay between diagnosis and treatment for female breast cancer patients in Alberta. Specifically, the following questions were addressed:

1) What are the mean and median waiting times in days between definitive diagnosis and treatment for female breast cancer patients in Alberta for each year from 1997-2000?

2) Was there a significant trend in delay over these years? It was hypothesized that there was no statistically significant increase in delay between diagnosis and treatment each year in the study period.

3) Do significant waiting time variations between definitive diagnosis and treatment exist amongst the 17 defined health regions in Alberta? It was hypothesized that there were no statistically significant differences in mean waiting times experienced by women from different Regional Health Authorities in Alberta.

4) Do the factors of age, stage, Regional Health Authority, Regional Health Authority category, community size at time of diagnosis, and year of diagnosis impact the delay interval between diagnosis and treatment experienced by female breast cancer patients in Alberta for the years 1997-2000? It was hypothesized that all of these factors were not associated with waiting time.

3.3 Alberta Cancer Registry

The Alberta Cancer Registry is a computerized data base of all new primary cancer incidents in the province and is operated by the Alberta Cancer Board's (ACB) Division of Epidemiology, Prevention and Screening. The inclusion of all cancer cases in this registry is mandated by Alberta statutes under the Cancer Registry Regulation of the *Cancer Programs Act* (58). Two centres are responsible for the collection of data. The Tom Baker Cancer Institute in Calgary is responsible for collecting cancer cases in the southern half of the province, while the Cross Cancer Institute in Edmonton maintains data collection for the northern half of Alberta (58).

Quality assurance projects conducted by the ACB have indicated that 95% of breast cancer incidents are recorded in the registry (58). Further support for the registry's validity and reliability has been the award of the Gold Standard for highest degree of data quality by the North American Association of Central Cancer Registries, which is a data quality organization (59). The certification is based on criteria that are evaluated each year. The criteria for the Gold Standard include that the registry be deemed 95% complete, the records are collected within 23 months and duplicate records are equal to or less than one in 1000 cases in the registry. The high quality of the data enables researchers to conduct valid and reliable population-based research.

3.4 Study Population

This population-based study consists of all women diagnosed with breast cancer in Alberta for the years of 1997-2000.

The mean number of Albertans residing in cities during the years of the study was 1 817 943, while the average official total population was 2 832 564 (Table 6) (60). Therefore, on average, approximately 35% of Alberta's population lived in rural communities. The large scale of the province and its high rural population directly impact the provision of health care. Only two tertiary centres within the province provide radiation and chemotherapy treatment and specialist follow up care (WW Cross Cancer Institute in Edmonton, RHA 10 and Tom Baker Cancer Centre in Calgary, RHA 4), five centres offer chemotherapy and follow up care (Fort McMurray, RHA 16; Grande Prairie Clinic, RHA 13; Lethbridge Clinic, RHA 1; Central Alberta Cancer Centre in Red Deer, RHA 6; and Medicine Hat Cancer Clinic; RHA 2), while ten centres provide only chemotherapy (Barrhead, RHA 11; Bonnyville, RHA 12; Camrose, RHA 7; Drumheller, RHA 5; High River, RHA 3; Hinton, RHA 8; Peace River, RHA 14; Lloydminster, RHA 7; and Bow Valley, RHA 3) (Table 7, Figure 3) (61).

Table 6: A summary of the Alberta population for the years of 1997-2000.

Population	**1997**	**1998**	**1999**	**2000**
City*	1 757 246	1 783113	1 851 449	1 879 962
Official Total	2 744 731	2 781 290	2 871 271	2 932 963
Female	1 407 411	1 440 171	1 465 495	1 490 571

*Cities include: Airdrie, Calgary, Camrose, Drumheller, Edmonton, Fort Saskatchewan, Grande Prairie, Leduc, Lethbridge, Medicine Hat, Red Deer, Spruce Grove, St. Albert, and Wetaskiwin (60).

Table 7: A summary of where in Alberta various cancer services are provided.

Type of Treatment Provided	**Locations in Alberta**
Radiation, chemotherapy, and specialist follow up	WW Cross Cancer Institute, Edmonton (RHA 10) Tom Baker Cancer Centre, Calgary (RHA 4)
Chemotherapy and specialist follow up	Fort McMurray (RHA 16) Grande Prairie Cancer Clinic (RHA 13) Lethbridge Cancer Clinic (RHA 1) Central Alberta Cancer Centre, Red Deer (RHA 6) Medicine Hat Cancer Clinic (RHA 2)
Chemotherapy	Barrhead (RHA11) Bonnyville (RHA 12) Bow Valley (RHA 3) Camrose (RHA 7) Drumheller (RHA 5) High River (RHA 3) Hinton (RHA 8) Lloydminster (RHA 7) Peace River (RHA 14)

3.5 Study Variables

After ethics approval was obtained, individual breast cancer data for the years of 1997-2000 were obtained from the Alberta Cancer Board. The variables obtained include: age of patient, stage of disease, date of diagnosis, date of treatment, postal code at time of diagnosis, and Regional Health Authority (RHA). The variables of interest in this study are age, stage, RHA, RHA category, community size of residence, year of diagnosis, and time between definitive diagnosis and treatment. Some of these variables were used directly from the obtained data (ie. age, stage and RHA), while others were computed and coded by the researcher using the given information (ie. RHA category, community size, and time between diagnosis and treatment). These variables were defined and coded as follows:

A) ***Age***: is defined in the registry and this study as the number of years old the patient was at diagnosis.

B) ***Stage***: is coded by the registry as 1, 2, 3, or 4 with each stage being considered more severe than the last. The stage is the result of an algorithm that searches the patient's chart for any pathological and clinical stage information. An aggregate stage (stage 1-4) is based on information regarding tumor size, involvement of lymph nodes and whether or not the cancer has metastasized (TNM components- tumor node metastasis). Stage 1 cancers involve tumors less than 2cm that have not spread; Stage 2 cancers are defined as tumors 2cm-5cm with or without spread to lymph nodes; Stage 3 cancers involve tumors >5cm with or without spread to

lymph nodes; and all cancers that have spread to other parts of the body are classified as Stage 4, regardless of size and lymph node involvement (62). If an aggregate stage (1-4) is found in the chart, it is used; however, if no aggregate stage is indicated, the algorithm is used to obtain stage from TNM components of stage indicated in the chart. If no staging information is found in the chart, no stage is indicated in the registry.

C) ***RHA***: is the health region the patient lived in at the time of her diagnosis. During the period studied, Alberta was divided into 17 health regions. These 17 RHAs were responsible for the hospitals and community and public health services within their designated borders. The population and resources of the health regions varied considerably. The registry used the 2001 boundaries to define RHA regardless of year(s) of data requested (Figure 2). No border changes during the period studied were identified.

D) ***RHA Category***: is an unofficial categorization of RHAs into those considered to be "urban", "rurban" and "rural". The category an RHA belongs to is based on the cancer services it can provide. An urban RHA is one that offers tertiary cancer treatment (radiation, chemotherapy and specialist follow up), a rurban RHA can provide secondary cancer treatment (chemotherapy and specialist follow up) and usually has a midsize community with surrounding rural communities within its boundaries, and a rural RHA has no secondary or tertiary treatment centre (Table 7). Of the 17 RHAs in Alberta, two were considered urban (#4

Calgary Health Region and #10 Capital Health Authority), five were considered rurban (#1 Chinook Health Region, #2 Palliser Health Authority, #6 David Thompson Regional Health Authority, #13 Mistahia Regional Health Authority, and #16 Northern Lights Regional Health Authority) and the other 10 were considered rural (Figure 2).

E) ***Community Size***: was categorized as residences consisting of more than 100 000 people, 10 000-100 000 people, and less than 10 000 people. The patient's postal code at time of diagnosis was converted to the specific residence using a Postal Code Converter Instrument obtained from Alberta Health and Wellness. In Alberta, only two communities have more than 100 000 residents and 17 have between 10 000 and 100 000 residents (Table 8).

F) ***Year of Diagnosis***: was considered as 1997, 1998, 1999, or 2000.

G) ***Time between Diagnosis and Treatment***: was calculated as the continuous number of days between the given dates for diagnosis and treatment. If the patient had more than one diagnostic test, the date of diagnosis recorded in the registry was the date of the last diagnostic test, which is considered to be the definitive diagnosis. The date of treatment was considered as the first day treatment was obtained. In almost all cases, the definitive treatment would be surgical intervention (either a mastectomy or a lumpectomy).

Age, stage, RHA, RHA category, population of residence, and year of diagnosis are the independent variables and the number of days between diagnosis and treatment is the dependent variable in this study.

Table 8: Cities included in the three population categories.

Population Category	**Alberta Cities Included**	
>100 000 residents	Calgary Edmonton	
10 000-100 000 residents	Airdrie Camrose Cochrane Drumheller Grande Prairie Lethbridge Medicine Hat Spruce Grove Wetaskiwin	Brooks Canmore Cold Lake Fort Saskatchewan Leduc Lloydminster Red Deer St. Albert
<10 000 residents	All other communities not mentioned above	

3.6 Statistical Methods

The data were analyzed using various statistical functions contained in the Statistical Package for the Social Sciences (SPSS) 11.0.

Prior to the analyses all variables were reviewed for accuracy of data entry, missing values, univariate and multivariate outliers, and fit between their distributions and the assumptions of multivariate analysis (including normality, linearity, homoscedasticity, and non-multicollinearity). Missing data determined to be random and less than 3% of the total sample were excluded, whereas non-random missing data were imputed using the missing data regression option of Linear Trend at Point in SPSS. Frequency distributions and Mahalanobis distance (distance of a case from the centroid of the remaining cases where the centroid is the point created by the means of all the variables) with $p<0.001$ were utilized to assess the presence of univariate and multivariate outliers, respectively (63). Histograms and values of skewness and kurtosis were used to determine normality of each variable's distribution. Data with moderate skewness (<2) or kurtosis (<5) were transformed using square root transformations. Data with excessive skewness (2-5) or kurtosis (>5) were altered using a log transformation. The assumptions of linearity and homoscedasticity were revealed by bivariate scatterplots of each pair of variables. Variables that did not portray a linear relationship with length of waiting time (RHA, age, stage) were recoded or collapsed into new categories that did indicate the assumed linear trend. RHA was dummy coded into a set of dichotomous variables. For example, cases were

considered either from RHA 1 or not, RHA 2 or not, RHA 3 or not and so on. Multicollinearity was identified using SPSS collinearity diagnostics. The criteria used to identify multicollinearity were a conditioning index of greater than 30 and two variance proportions greater than 0.5, as suggested by Tabachnik and Fidell (63).

Descriptive statistics were used to illustrate waiting times from diagnosis to treatment for the population over the entire period of the study, for each year, and for various subgroups of each independent variable. The means and medians were both reported, but the medians were used more for graphing because this measure of central tendency is less subject to bias from extreme cases. To determine if significant differences in the waiting times for women in different subgroups of each variable (age, stage, community size, RHA group, year of study and RHA) existed, the nonparametric Kruskal Wallis test was used. If the test indicated that there was a significant difference, Dunn post hoc tests were used to specify the groups that had significant variations in waiting time. For the "stage missing" versus "stage not missing variable", a Mann-Whitney U test was used because there were only two independent samples to compare. Nonparametric tests were used instead of the parametric analysis of variance (ANOVA) or independent t-tests because of unequal sample sizes in each category being compared.

Finally, standard multiple linear regression was used to examine the correlates of waiting time between diagnosis and treatment for breast cancer patients using the following variables as predictors: age, stage, RHA, community

size, and year of diagnosis. A decision was made not to include RHA category as a predictor variable because of likely high multicollinearity with RHA. Standard regression was chosen because there was no theoretical basis for choosing either sequential or stepwise variable entry. To ensure that important variables are entered into and not excluded from the model, the default probability of F at entry was altered from 0.05 to 0.10 and the exit value changed from 0.10 to 0.15, which was also suggested by Tabachnik and Fidell (63). Two separate regressions were run using different methods for dealing with the missing data to determine if the missing data was a good predictor itself. First, a new and predictor variable was created for "missing stage" versus "stage not missing" and the missing values in the original stage variable were imputed using SPSS Linear Trend at Point. Secondly, the analysis was repeated using only complete cases.

After examining the results from the univariate and multivariate analyses, it was decided to repeat the regression using a dichotomized south or north RHA variable instead of dummy coded RHA variables. RHAs 1-6 were considered southern, while RHAs 7-17 were considered northern. An independent t-test was also used to test for significant differences between mean waiting times of southern and northern RHA patients. A parametric test was chosen because both groups had a similar number of women.

3.7 Summary

This chapter provided brief justification for this study based on the findings from the literature presented in the previous chapter. It was noted that

there is a lack of studies examining system delay and that components of system delay should be independently assessed.

This chapter also presented the objective and specific research questions of the study. This study will determine baseline waiting time data for Alberta breast cancer patients and examine the effect that age, stage, RHA, RHA category, population, and year of diagnosis have on length of waiting time between diagnosis and treatment in Alberta.

The data source (ie. the Alberta Cancer Registry) was described in terms of who collects the data, the reliability of it and the variables it contains. Although relatively few variables are available, the strength of the data is that is it very reliable and represents the population of breast cancer patients in Alberta.

Finally, this chapter described the statistical methods that were employed to answer the research questions. Descriptive, nonparametric and multivariate procedures were used. Standard multiple regression was used to build a predictor model of delay and indicate the relative importance of variables for the prediction of waiting time.

The following chapter will present the results from the analyses. It will statistically describe the population; waiting time data for the population and various subgroups; the groups that have significantly different waiting times; and the regression model.

CHAPTER 4: RESULTS

4.1 Overview

The previous chapter outlined the research questions, defined the study variables and discussed the statistical methods employed. The purpose of this chapter is to present the results from the analysis. It will describe the study sample and the data screening and cleaning conducted prior to analysis. Finally, it will illustrate the univariate and multivariate test results.

4.2 Sample

Over the 4-year study period, there were a total of 6418 female breast cancer cases recorded in the Alberta Cancer Registry. There were 1578 cases (24.6%) in 1997, 1482 cases (23.1%) in 1998, 1687 cases (26.3%) in 1999, and 1671 (26%) cases in 2000.

A description of characteristics of the study population is presented in Table 9. The mean age of the breast cancer patients was 60.5 (SD=14.4) ranging from 10 to 99 years of age. Those cases under the age of 20 were later removed (see section 4.3). The 51-60 years age group represented the largest percent of the population (23.2%). Fewer than 10% of the patients had stage 3 or 4 disease and

Table 9: A summary of the characteristics of the study population.

Variable	Total no. (and %)	1997 (%)	1998 (%)	1999 (%)	2000 (%)
Age Group					
<30	37 (0.6)	0.5	0.5	0.5	0.7
31-40	473 (7.4)	7.2	8.0	7.7	6.6
41-50	1329 (20.7)	20.8	21.4	19.5	21.2
51-60	1486 (23.2)	23.4	21.0	23.8	24.2
61-70	1301 (20.3)	19.2	21.1	21.6	19.2
71-80	1184 (18.4)	19.5	18.3	17.9	18.2
81-90	541 (8.4)	8.3	8.6	8.3	8.6
>90	67 (1.0)	1.1	1.1	0.8	1.3
Stage					
1	2348 (36.6)	34.5	36.8	36.2	38.7
2	2169 (33.8)	31.8	33.9	35.1	34.3
3	386 (6)	6.5	6.2	5.8	5.6
4	207 (3.2)	3.7	3.4	3.0	2.8
unknown	1308 (20.4)	23.4	19.7	19.8	18.7
RHA Category					
1	345 (5.4)	5.5	5.6	5.2	5.3
2	187 (2.9)	3.0	3.0	2.7	2.9
3	165 (2.6)	2.9	3.2	2.4	1.9
4	1981 (30.8)	30.0	29.1	31.9	32.1
5	147 (2.3)	2.2	2.6	2.0	2.5
6	405 (6.3)	6.7	5.4	6.2	6.9
7	253 (4)	4.1	3.8	3.6	4.2
8	177 (2.7)	3.0	3.4	2.5	2.3
9	66 (1)	0.9	0.9	1.3	1.0
10	1973 (30.8)	29.8	31.5	31.6	30.1
11	204 (3.2)	3.6	3.0	3.6	2.5
12	191 (3)	3.5	2.6	2.4	3.5
13	175 (2.7)	2.1	3.6	2.5	2.8
14	52 (0.8)	0.8	0.7	0.8	0.9
15	33 (0.5)	0.7	0.8	0.2	0.4
16	48 (0.8)	1.0	0.6	0.9	0.4
17	16 (0.2)	0.3	0.1	0.3	0.4
RHA Category					
Rural	1302 (20.3)	21.9	21.1	18.9	19.4
Rurban	1162 (18.1)	18.3	18.3	17.6	18.3
Urban	3954 (61.6)	59.8	60.6	63.6	62.3
Community Size					
<10 000	2582 (40.2)	41.9	41.2	38.2	39.9
10 000- 100 000	625 (9.8)	9.5	9.5	9.3	10.7
>100 000	3211 (50.0)	48.6	49.3	52.5	49.4

there was a small decrease in the percent of these more severe cases over the period of the study. Overall, nearly 19% of cases did not have a recorded stage. Fifty percent of the women lived in an urban RHA at time of diagnosis. Only 9.8% of cases were from an area of residence with a population between 10 000-100 000, while 40.2% were from an area with <10 000 people.

4.3 Data Screening and Analysis of Multivariate Assumptions

Prior to analysis, all variables were reviewed for accuracy of data entry, identification of missing values and outliers, and the fit between their distributions and the assumptions of multivariate analysis, including normality, linearity, homoscedasticity, and non-multicollinearity.

Of the 6418 cases, 180 cases (<3% of total data) did not have a recorded waiting time. The waiting time for these cases was missing either because it was not recorded in the data base or because the date of treatment was recorded as occurring before the date of diagnosis. The 180 missing values were deemed to be random and constituted a very small portion of the population and, thus, were deleted from further analyses. After deletion of these cases, it was established that 1169 cases (19% of total data) had a missing stage variable. An independent *t*-test indicated that those with a stage were significantly older than those with no recorded stage ($t=19.9$, $p<0.001$); therefore, the missing data were not random. Because of the possibility that missing stage values could be good predictors of waiting time, two separate regressions were run using different methods for dealing with the missing data. First, a new variable was created for missing stage

versus stage not missing and the missing values in the original stage variable were imputed using SPSS Linear Trend at Point. Secondly, the analysis was repeated using only complete cases. No other variables presented missing data.

Univariate and multivariate outliers were determined through examination of each variable's distribution and the Mahalanobis distances for each case with $p<0.001$, respectively. The frequency distribution of age showed two outlying cases under the age of 20. Both of these cases were deleted from the analysis due to suspicion that they were originally entered into the data base incorrectly. No other outliers were identified.

The individual variables were screened for normality through histograms and values of skewness and kurtosis. Waiting time was severely skewed due to the large number of women who received treatment the same day as their diagnosis. A logarithmic transformation normalized this variable. The moderate skewness of stage was corrected with a square root transformation. The other variables demonstrated histograms and values of skewness and kurtosis that approximated the normal distribution.

The assumptions of linearity and homoscedasticity were revealed by bivariate scatterplots of each pair of variables. Age group, and stage portrayed a non-linear relationship with log waiting time. Subsequently, these variables were recoded into groups that did demonstrate a linear trend. Stage was dichotomized into those cases diagnosed with Stage 1 disease versus those with Stage 2, 3 or 4. Similarly, age was collapsed into those patients 70 years and younger, 71-80, 81-

90, and older than 90 years. RHA was dummy coded into a set of dichotomous variables. For example, women were considered to be either from RHA 1 or not.

Screening for multicollinearity and singularity was accomplished using SPSS collinearity diagnostics in which conditioning indexes and variance proportions are produced for each variable. No variables had an index greater than 30 or a variance proportion greater than 0.5, which Tabachnik and Fidell define as criteria of multicollinearity (63).

4.4 Descriptive Statistics and Univariate Analyses

Tables 10-13 and Figures 4-11 present variations in time from definitive diagnosis to definitive treatment for various subgroups of the six independent variables. The overall mean waiting time was 20.2 days (SD = 21.6), while the median was 17 days. The waiting time ranged from 0 days to 243 days (Table 10). Nearly 27% of women (1709) began treatment the same day as their diagnosis (0 days). Only 43.8% of the population was treated within the recommended 14 days established by the Canadian Society for Surgical Oncology (CSSO). Ninety percent of women were treated within 43 days of their diagnosis.

For purposes of reporting, age was categorized into those cases: <31, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90, or >90. There is variation in the mean and median waiting times of women in different age groups, which is illustrated in Table 10 and Figure 5. The median waiting times for the 51-60 and 61-70 age groups were both 19 days (means of 21.5 and 20.8 days, respectively) , while the >90 age group experienced a median delay of 0 days (mean of 18.6 days). A

Kruskal Wallis test indicated significant differences in the medians of waiting times of women in different age groups ($H=87.954$, $p<0.001$). Dunn post hoc tests determined that those younger than 70 waited, on average, significantly longer than each of the older age groups ($p<0.05$). Similarly, women who were 71-80 years old waited, on average, appreciably longer than the two older age groups. A separate analysis of those cases with zero days between diagnosis and treatment was conducted to establish if there was an association with age. Table 11 demonstrates that from the 41-50 year age group through to the oldest group, there was a steady increase in the percent of women who did not wait to receive treatment.

Table 10 and Figure 6 present the waiting time distribution by stage of disease and reveal that women with stage 1 wait the longest for treatment. Women with stage 1, 2, 3, and 4 disease experienced a median (and mean) delay of 20 days (22.1 days), 15 days (17.5 days), 14 days (18.2 days), and 14 days (18.5), respectively. Cases with no recorded stage waited a median of 18 days and a mean of 22.4 days. The Kruskal Wallis test indicated that there was a significant difference in the median waiting times of women diagnosed with different stages of breast cancer ($H= 82.140$, $p<0.001$). Dunn post hoc comparisons specified that women with no recorded stage or with stage 1 disease waited, on average, significantly longer than all other stages ($p<0.05$). No other stages demonstrated significant waiting time differences. The Mann-Whitney U test indicated that there was no significant difference in waiting times for women with and without a recorded stage ($U=2883254$, $p=0.138$).

There was little variation in the mean and median waiting times of women from different community sizes, as portrayed in Table 10 and Figure 7. Women from communities with less than 10 000 residents waited a median of 18 days and a mean of 20.4 days. The two larger community sizes of 10 000-100 000 and >100 000 residents presented median waiting times of 17 days and respective mean waiting times of 19.5 and 20.1 days. The Kruskal Wallis test indicated that there was no significant difference in the median waiting times of women from different community sizes (H= 1.791, p=0.408).

Table 10 and Figure 8 describe the waiting time distribution by RHA group and illustrate variation in waiting times associated with the different groups. Women living in an urban, rurban or rural RHA experienced a median (and mean) delay of 17 days (20.5 days), 14 days (18.0 days), and 19 days (21.5 days), respectively. The Kruskal Wallis test indicated that there was a significant difference in the median waiting times of women from different RHA categories (H= 30.439, p<0.001). Dunn post hoc comparisons specified that women who lived in rurban RHAs waited, on average, significantly less than women in rural or urban RHAs (p<0.05).

There was a yearly trend of increased mean and median waiting times, which is demonstrated in Table 10 and Figures 9 and 10. The median and mean waiting times increased by an average of two days each year of the study. The Kruskal Wallis test indicated that there was a significant difference in the median waiting times of women diagnosed in different years (H=86.199, p<0.001). Dunn post hoc tests specified that women diagnosed in 1997 waited, on average,

significantly less than women diagnosed in 1999 or 2000 and women diagnosed in 1998 or 1999 waited significantly less than women diagnosed in subsequent years ($p<0.05$). Furthermore, the percentage of women waiting more than two weeks for treatment increased each year from 49.7% in 1997 to 63.9% in 2000 (Figure 9).

Waiting times also varied in different RHAs (Tables 12 and 13 and Figure 11). The median and mean waiting times ranged from 11 days to 22.5 days and from 15.4 days to 28.6 days, respectively. The Kruskal Wallis test indicated that there was a significant difference in the median of waiting times of women from different RHAs at diagnosis ($H= 160.056$, $p<0.001$). Dunn post hoc tests specified that women living in RHA 1 experienced significantly less delay than those from RHAs 7, 9, 10, 11, 12, and 13, women from RHA 2 less than those from RHAs 10 and 12, women from RHA 4 less than those from RHAs 10, 12, and 13, and women from RHA 6 less than those from RHAs 9, 10, 12, and 13. An independent t-test indicated that women from southern RHAs waited, on average, significantly less than women from northern RHAs ($t= 9.101$, $p<0.001$) (Table 10, Figure 12). Box plots showing the 95% confidence intervals of the log waiting times for each RHA also portrays that Southern RHAs are generally lower than the population mean waiting time, while the Northern RHAs are generally higher (Figure 13).

Table 10: Waiting time from diagnosis to treatment initiation for breast cancer patients in Alberta for the years of 1997-2000.

Characteristic	No. of Episodes (n)	Median Wait Time (d)	Mean Wait Time (d)	90th percentile wait time (d)	% women waiting >14 days
Age group (yr)					
<31	34	16	22.3	48	54.5
31-40	468	15	18.4	38	50.2
41-50	1306	17	20.9	44	58.5
51-60	1460	19	21.5	43	62.1
61-70	1273	19	20.8	44	59.0
71-80	1143	16	19.2	43	52.7
81-90	502	6	17.6	46	41.7
>90	52	0	18.6	45	34.6
Stage					
Unknown	1169	18	22.4	51	56.7
1	2333	20	22.1	44	62.6
2	2158	15	17.5	40	50.8
3	377	14	18.2	42	49.9
4	201	14	18.5	36	47.5
Population					
<10 000	2510	18	20.4	43	56.9
10 000-100 000	609	17	19.5	43	55.2
>100 000	3119	17	20.1	44	55.8
RHA Group					
Urban	3848	17	20.5	44	57.4
Rurban	1125	14	18.0	42	48.6
Rural	1265	19	21.5	44	59.4
Year of Study					
1997	1521	14	17.9	40	49.7
1998	1447	16	18.2	39	51.8
1999	1651	18	20.9	44	58.3
2000	1619	20	23.6	50	63.9
RHA Position					
South	3144	14	17.8	41	48.4
North	3094	20	22.7	46	64.1

Table 11: A description of the number and percentage of women, by age group, waiting zero days for breast cancer surgery in Alberta between 1997 and 2000.

Age Category	Number of Women Waiting 0 days	% of Women Waiting 0 days
<31	6	18.2%
31-40	115	24.6%
41-50	274	21.0%
51-60	315	21.6%
61-70	342	26.9%
71-80	386	33.8%
81-90	241	48.1%
>90	30	57.7%

Table 12: Waiting time from diagnosis to treatment for breast cancer in each RHA in Alberta between the years of 1997 and 2000.

RHA	No. of Episodes (n)	Median Wait Time (d)	Mean Wait Time (d)	90th percentile wait time (d)	% women waiting >14 days
1	338	13	15.4	34	43.8
2	182	11	20.2	47	48.7
3	161	14	18.1	43	46.6
4	1928	14	18.1	43	49.3
5	144	17	19.4	45	54.9
6	390	12.5	16.1	39	45.6
7	245	20	22.7	47	60.8
8	172	17.5	18.9	37	58.7
9	66	22.5	22.4	47	65.2
10	1919	20	22.8	46	65.5
11	201	19	23.3	50	60.7
12	182	21.5	22.5	44	68.7
13	167	21	24.8	55	63.5
14	50	17	25.1	61	60.0
15	31	21	28.6	49	58.1
16	46	15	18.3	30	54.3
17	15	13	23.4	73	40.0

Table 13: Waiting time from diagnosis to treatment for breast cancer in each RHA in Alberta for each year from 1997-2000.

RHA	**Wait times** n, median (d) **1997**	**Wait times** n, median (d) **1998**	**Wait times** n, median (d) **1999**	**Wait times** n, median (d) **2000**
1	85 (9)	80 (11.5)	87 (14)	86 (14)
2	47 (0)	44 (5.5)	44 (10.5)	47 (23)
3	45 (19)	45 (8)	40 (10.5)	31 (20)
4	455 (13)	424 (14)	529 (13)	520 (19)
5	33 (11)	38 (14)	33 (17)	39 (21)
6	97 (2)	79 (14)	102 (12.5)	112 (15.5)
7	65 (17)	55 (21)	60 (18.5)	65 (23)
8	46 (19.5)	50 (15.5)	39 (19)	37 (17)
9	14 (24.5)	14 (7.5)	22 (18)	16 (24)
10	452 (16)	454 (17)	521 (21)	492 (21)
11	57 (19)	45 (14)	58 (19.5)	41 (26)
12	52 (20)	36 (21)	39 (22)	55 (22)
13	31 (9)	49 (18)	40 (27.5)	47 (21)
14	12 (14)	11 (13)	12 (28.5)	15 (20)
15	10 (26.5)	12 (24)	3 (15)	6 (16)
16	15 (16)	9 (14)	16 (18.5)	6 (22)
17	4 (1)	2 (13)	5 (3)	4 (60)

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4.5 Multivariate Analysis

Multivariate modeling using linear regression in SPSS was used to produce estimates of the independent effect of age, stage, stage missing, RHA, community size, and year of diagnosis in a predictor model for the system delay interval of diagnosis to treatment. The predictor variables were entered simultaneously.

The regression that computed a new variable of stage missing versus present resulted in a slightly larger value of variance accounted for; therefore, only the results from the regression that imputed the missing stage values is presented. Table 14 displays the correlations between the variables. Table 15 displays the unstandardized regression coefficients (B), the standardized regression coefficients (β), the semi-partial correlations (sr_i^2), the amount of variation in waiting time accounted for by the predictor variables (R^2), and adjusted R^2. R for regression was significantly different from zero ($F = 29.396$, $p<0.001$). Four of the five non-dummy coded variables contributed significantly to the prediction of wait time as logarithmically transformed: age ($sr_i^2= 0.026$), stage ($sr_i^2= 0.014$), stage missing versus stage recorded ($sr_i^2= 0.010$), and year of diagnosis ($sr_i^2= 0.012$). Eleven of the RHA dummy coded variables also significantly contributed to the prediction of log waiting time: RHA 6 ($sr_i^2=$ 0.002), RHA 7 ($sr_i^2= 0.004$), RHA 8 ($sr_i^2= 0.002$), RHA 9 ($sr_i^2= 0.001$), RHA 10 ($sr_i^2= 0.024$), RHA 11 ($sr_i^2= 0.005$), RHA 12 ($sr_i^2= 0.006$), RHA 13 ($sr_i^2= 0.003$), RHA14 ($sr_i^2=$ 0.001), RHA15 ($sr_i^2=$ 0.001), and RHA 16 ($sr_i^2=$ 0.001). Altogether, 9% (8.7% adjusted) of the variability in waiting time from diagnosis

to treatment for Alberta breast cancer patients was predicted by knowing the scores on all six predictor variables.

Because the significant waiting time variations appeared to be between Southern and Northern RHAs, a second regression using a dichotomized South (RHAs 1-6) or North (RHAs 7-17) RHA variable was performed. There was no increase in the amount of variation accounted for (R^2= 0.087).

Table 14: The correlation values for all pairs of variables entered into the linear regression analysis.

Variables	Age	RHA	Stage	Stage Missing	Community Size	Year of Diagnosis
Time	-.145**		-.110**	.004	.013	.102**
Age			.086**	-.264**	.008	.008
RHA						
Stage				-.371**	-.001	-.026*
Stage Missing					-.029*	.036**
Community Size						-.023
Year of Diagnosis						

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

Table 15: Standard multiple regression using RHAs, age, stage, stage missing or recorded, community size and year of diagnosis as predictor variables of log waiting time from diagnosis to treatment for breast cancer patients.

Variable	**Regression Coefficients (B)**	**Standardized Regression Coefficients (β)**	**Squared Semi-Partial Correlations (sr_i^2)**
RHA 1 dummy	-0.005	-0.002	0.000
RHA 2 dummy	-0.019	-0.005	0.000
RHA 3 dummy	0.075	0.018	0.000
RHA 5 dummy	0.039	0.009	0.000
RHA 6 dummy	-0.113**	-0.042	0.002
RHA 7 dummy	0.232**	0.069	0.004
RHA 8 dummy	0.196**	0.049	0.002
RHA 9 dummy	0.185*	0.029	0.001
RHA 10 dummy	0.260**	0.184	0.024
RHA 11 dummy	0.274**	0.074	0.005
RHA 12 dummy	0.320**	0.083	0.006
RHA 13 dummy	0.227**	0.056	0.003
RHA 14 dummy	0.189*	0.026	0.001
RHA 15 dummy	0.280*	0.030	0.001
RHA 16 dummy	0.211*	0.028	0.001
RHA 17 dummy	0.029	0.002	0.000
Age	-0.165**	-0.169	0.026
Stage	-0.169**	-0.126	0.014
Stage missing/ present	-0.187**	-0.112	0.010
Community Size	-0.0006	-0.006	0.000
Year of diagnosis	0.006**	0.107	0.012

$R^2 = 0.090$**, adjusted $R^2 = 0.087$.
** $p<0.01$, * $p<0.05$

Note: RHA was dummy coded into a set of dichotomous variables and age and stage were recoded to provide variables that demonstrated linear relationships with waiting time. Age was collapsed into patients <70 and all other older groups remained the same. Stage was transformed into cases with stage 1 cancer versus those with stage 2, 3, 4 or missing (which was imputed using SPSS Linear Trend of Point).

4.6 Summary

The median waiting time from diagnosis of breast cancer to treatment in Alberta was 17 days for the period 1997 to 2000. The mean and median waiting times increased each year of the study by an average of two days. Furthermore, the majority of women were not treated within the recommended 14 days after diagnosis. Each year, the percentage of patients not treated within this recommended time increased by an average of 4.7%.

Very little (9%) of the variation in the waiting time between diagnosis and breast cancer treatment was explained by the developed model. The relative importance of predictors of delay was found to be: living in RHA 10 at diagnosis, age at diagnosis, stage of breast cancer, stage missing or recorded, year of diagnosis, followed by several other significant RHAs.

Univariate and multivariate analyses indicated that there was significant variation in waiting times for women from different RHAs at time of diagnosis. Further examination portrayed that women from southern RHAs (1-6) waited, on average, significantly less than women from northern RHAs (7-17). Univariate analysis indicated that women from rurban RHAs experienced less delay than women from rural and urban RHAs, but no significant difference was found between rural and urban patients.

Women who were less than 70 years old at diagnosis waited significantly longer to be treated than women who were older. Older age was also associated

with an increased likelihood of receiving a diagnosis of breast cancer and treatment on the same day.

Patients diagnosed with Stage 1 disease waited significantly longer for treatment than women with Stage 2, 3 or 4 disease. Univariate and multivariate analyses confirmed that no difference in the waiting times for women with Stage 2, 3, or 4 existed. Multivariate regression indicated that women with no recorded stage waited significantly longer than women with a staged disease.

The following chapter will discuss these findings. It will provide specific answers to the research questions presented in Chapter 3. I will present possible explanations for the results pertaining to each variable and compare the findings of this study to similar studies encountered in the literature review. Finally, it will recognize the limitations and strengths of the study and make recommendations for future research.

CHAPTER 5: DISCUSSION AND CONCLUSIONS

5.1 Introduction

The previous chapter presented the results from the statistical analysis. The purpose of this chapter is to discuss the findings of this study. It will provide answers to the research questions outlined in Chapter 3, discuss the findings with respect to each variable and compare the results to those identified in the literature review. Furthermore, it will recognize the limitations and strengths of the study and present ideas for future research.

5.2 Research Questions Answered

Q1: *What are the mean and median waiting times in days between definitive diagnosis and treatment for female breast cancer patients in Alberta for each year from 1997-2000?*

A1: The overall mean and median waiting times for breast cancer surgery in Alberta was 20.2 days and 17 days, respectively. In 1997 the mean was 17.9 days and the median was 14 days; in 1998 the mean was 18.2 days and the median was 16 days; in 1999 the mean was 20.9 days and the median was 18 days; and in 2000 the mean was 23.6 days and the median was 20 days.

Q2: *Was there a significant trend in delay over these years?*

A2: Dunn post hoc tests specified that there was a significant increase in the mean waiting time each year from 1998-2000 ($H=86.199$, $P<0.001$).

Q3: *Do significant waiting time variations between definitive diagnosis and treatment exist amongst the 17 defined health regions in Alberta?*

A3: Significant variations in waiting times for women from different RHAs at diagnosis were indicated by Dunn post hoc tests. Women from Southern RHAs (1-6) experienced, on average, significantly less delay than women from Northern RHAs (7-17). Furthermore, women who were residents of rurban RHAs waited, on average, significantly less than women from urban and rural RHAs.

Q4: *Do the factors of age, stage, regional health authority, regional health authority category, community size at time of diagnosis, and year of diagnosis impact the delay interval between diagnosis and treatment experienced by female breast cancer patients in Alberta for the years 1997-2000?*

A4: Age, stage, RHA, and year of diagnosis were significant predictors of waiting time in multivariate analysis. RHA category, which was not included in the multivariate model, was significantly associated with waiting time in the univariate analysis.

5.3 Discussion of Findings

Given the evidence that long delays can negatively impact the survival of breast cancer patients, one major purpose of this study was to determine waiting time from diagnosis to treatment and compare the length to other literature reports

and recommended guidelines. There are methodological obstacles to a direct comparison between the median wait time result in this study with other studies because of the numerous definitions of delay intervals and differences in the health care systems. The median of 17 days between diagnosis and treatment in Alberta established by this study is higher than the 10 days reported by an American study (28) and lower than two Canadian studies that reported 20 days between treatment decision and treatment in Ontario (32) and 24 days between diagnostic procedure to treatment in Quebec (29). The differences in the American and Canadian health care systems could account for the first discrepancy. The nature of American health service delivery leads to more capacity and the ability of insured patients to be treated quickly. Whereas in Canada, capacity is often maximally utilized and wait lists are common. Further examination and comparison of care pathway structure in Alberta, Quebec, and Ontario would have to be conducted before rationalizing the differences in the waiting times of these provinces.

The proportion of patients receiving treatment within the Canadian Society for Surgical Oncology (CSSO) recommended 14 days after diagnosis was 43.8% (33). Although this is higher than the 32.5% of cancer patients meeting the guideline reported in Ontario by Simunovic et al (32), it is unacceptable that the majority of women are not treated within the time set by an expert group. The recommendation of 14 days may not be sufficiently emphasized or practiced by physicians as it may seem unattainable. It is important to note that this is a recommended guideline not based on evidence that treating patients within two

weeks improves survival. Studies need to be conducted to elucidate the optimal time in which breast cancer patients should be treated.

The second major purpose of this study was to determine factors that predicted variation in waiting times. The regression model developed using characteristics of the patient (including age, stage of disease, stage recorded or missing, RHA, community size, and year of diagnosis) explained 9% of the variation in waiting times. Even though the variation accounted for was small, six of the seven variables were significant predictors of delay and potentially modifiable.

Age at diagnosis was the variable most consistently associated with system delay in the literature and in this study. Of the nine studies that examined the impact of age on provider delay, two reported no significant relationship between age and delay (17, 32), while seven reported that younger age was predictive of longer waiting times (12, 22, 28, 41, 46, 54, 5). Consistent with most of the literature, both univariate and multivariate analysis indicated that patients younger than 70 years old were more likely to experience longer waiting times than older patients. Sainsbury et al suggested that the association is due to physicians not expecting younger patients to have breast cancer because their risk is inherently lower (22). However, this explanation does not likely account for the finding in this study because women were already diagnosed and physicians would likely expect some women under 70 years of age to have cancer. Another possibility presented was that age is associated with delay because older women generally have more advanced disease. Again, this idea is not supported by this

study because the multiple regression indicated that age contributed independently to the prediction of waiting time. It is more likely that the difference can be attributed to the finding that older patients were more likely to be treated on the same day as their diagnosis, which would reduce the overall group mean. Age may contribute to the surgeon's choice to proceed to a definitive procedure immediately rather than subject an older patient to risks associated with multiple surgeries. Furthermore, it is likely that there are cosmetic considerations in the treatment decision of younger women and not with older women, allowing surgeons the freedom to perform the surgical treatment the day of the diagnosis. It is also possible that patient delay confounds the noted variation. Younger women might take longer in deciding between treatment options, leading to a perceived increase in system delay. The doubling time of breast cancer is quite long and based on this Dr. Susan Love's Breast Book recommend that patients take their time deciding their treatment (64). In order to verify these ideas and determine other possible accounts for the relationship between age and stage, further research needs to be conducted. It would be beneficial to begin with qualitative discussions with surgeons and other providers to elucidate their opinions on possible causes.

Stage was also significantly associated with waiting time. Univariate and multivariate analyses specified that women diagnosed with Stage 1 disease waited significantly longer for their treatment than women with either Stage 2, 3 or 4 disease. This finding was unexpected because Stage 1 and 2 are considered early stages of breast cancer, while Stage 3 and 4 are regarded as advanced disease.

Although studies have not specifically addressed the impact of stage, several did find the absence of a lump increased system delay (37, 41, 46, 54). Because Stage 1 is defined by a tumor smaller than two centimeters (along with other factors) it is possible that some of these lumps would not be palpable allowing for comparison to results reported by other studies. For example, Caplan et al suggested that because lumps are the classical symptom of breast cancer, physicians expedited the care pathway when women presented this symptom. It is unlikely that this explains the association in this study because women were already diagnosed. One plausible interpretation is that the treatment decision for women with stage 1 is more difficult, leading to an increase in waiting while the patient and the physician agreed upon the surgical intervention. This does not explain why the univariate analysis indicated that stage 2 patients do not experience significantly more delay because their treatment options are similar to those for stage 1 patients. It is possible that stage was not accurately recorded in the data base, resulting in misclassification. Before further interpretation of the relationship between waiting time and stage, it is recommended that the reliability of the stage variables within the Alberta Cancer Registry be assessed by auditing patient charts.

Multivariate analysis indicated that the absence of a recorded stage was predictive of delay, while univariate analysis did not portray a significant relationship. The contradictory findings could be the result of increased difficulty in proving significance with the nonparametric test used in the univariate analysis. No other studies reported interpretations of missing data. It is difficult to

speculate why women with no recorded stage on average waited longer for treatment because it is unknown why the stages were missing in the registry. Stage could be missing either because it is unknown or because it was not recorded in the chart from which the registry collects the data. A chart audit of patients with no recorded stage would help provide explanations for this finding.

The RHA that the women lived in at diagnosis was also significantly associated with waiting time. Other studies have reported significant regional differences in other jurisdictions (27, 28, 30, 54). Tests specified that it was RHAs 1, 2, 4, and 6 that had significantly lower waiting times. These RHAs are all situated in southern Alberta and have at least a secondary cancer treatment centre. The Northern and Southern disparity was confirmed by a separate univariate analysis. Although the number of cases in the South and North are similar (3143 patients versus 3093 patients, respectively), four of the six southern RHAs have at least a secondary treatment centre compared to only two of 11 Northern RHAs (Figure 2). Furthermore, three of the four secondary treatment centres are in Southern Alberta. It is feasable that the difference in waiting times in Southern and Northern Alberta was accounted for by the disproportionate number of secondary cancer treatment centres and capacity to initially manage breast cancer patients. This suggests that the secondary treatment centres reduce the demand on tertiary centres (RHAs 4 and 10) to provide treatment to women from surrounding RHAs. This explains the significant difference in the waiting times of RHA 4 and 10. However, it is not possible from this study to conclude whether the South does have more capacity to treat as a result of more treatment

centres because access to surgery is not related to existence of secondary centres. The first definitive treatment for most breast cancer cases will be surgery, which can occur outside of the cancer treatment centres. Therefore, it may be due to ecological fallacy that it appears that secondary centres are associated with reduced waiting times. The efficiency of the care pathway services could account for the disparity between the South and North. A comparison of the capacity (ie. specialists, surgeons, hospital beds, and other treatment resources) and the structure of the care pathway in Southern and Northern Alberta would help confirm if one or both of these explain the variation.

Further support for the suggestion that secondary cancer treatment centres result in reduced delay was provided by the univariate analysis that indicated patients from rurban RHAs experienced significantly less delay than patients from urban and rural RHAs. RHAs were considered rurban if they had a secondary treatment centre within their boundaries. No significant difference in the delay of women from urban and rural RHAs was discovered. This finding was also confirmed by the lack of significance of community size in univariate and multivariate analyses. Caplan et al found that rural women were treated faster than urban patients, however, it is difficult to compare these findings because of the different definitions of rural and urban (28). It was an encouraging finding because it suggests that there is equal access for rural patients to health services that are centralized in larger communities.

The final significant predictor of delay was the year in which women were diagnosed. Alarmingly, the median and mean waiting time for treatment

increased by an average of two days each year from 1997-2000. This is consistent with the study by Mayo et al that reported continual increases in waiting times for breast cancer patients in Quebec from 1992-1998 (29). The authors suggested that the annual increases in incidence of breast cancer and the aging population had resulted in more women requiring treatment for breast cancer, but resources had not increased accordingly, thereby, leading to longer delays. The absolute number of cases in this study did not increase each year. Therefore, the increased demand for treatment does not explain the average annual increase of two days. It was hypothesized that a decrease in the number of patients being treated the same day as their diagnosis because of changes in practice could account for the increase. A separate analysis of only those patients that waited one or more days for treatment disproved this idea, as the number of patients not waiting and the mean still increased each year. It is possible that the increase is spurious. Because we are only examining one portion of system delay, it does not indicate if the entire system delay period (from first physician visit to treatment) is increasing each year. It would be valuable to study the entire system interval as well as subintervals to determine if there are other trends of increase. It is recommended that the Alberta Cancer Registry include other significant dates of the care pathway in the database to facilitate further examination.

Although there were five significant predictors of delay, the amount of variance accounted for by these variables was only nine percent. The inclusion of other variables could have explained more of the variation in waiting times. There was some evidence in the literature review that presenting symptom,

socioeconomic status (SES) and ethnic origin/race could influence the system delay interval (Table 5). Because this study examined the period after diagnosis, it is unlikely that presenting symptom would have influenced the waiting time. Studies examining the impact of SES and race on delay have been conducted in the United States and should be examined within the context of the Canadian medical system given the diversity of the population. Again, it would be important for the Alberta Cancer Board to collect this information.

Likely environmental factors not included in the study or presented in the literature that could impact the delay interval are the specific treatment centre, surgeon providing the treatment, whether or not the patient was referred to a specialist or another surgeon for a second opinion, type of treatment, and travel distance. Treatment centres may impact waiting times because of differences in practice structure or capacity, which includes resources like the number of beds, operating rooms and surgeons. The treating surgeon also likely influences the waiting time because of dissimilarities in practice and available surgical operating time. Being referred to a specialist for treatment discussions or for a second opinion is another step in the care pathway that likely increases delay. The type of surgery that a woman receives could impact delay because of where specific treatments are offered and availability of these centres. It is possible that travel distance impacts waiting times in Alberta because of the centrality of treatment centres and the large area of the province. Examining these factors could help explain more of the waiting time variation.

5.4 Limitations and Strengths of Study

This study had a number of potential weaknesses. Other potential predictors could have been included to explain the variation in waiting time. This was a result of limited variables available in the Alberta Cancer Registry data base. It would have been beneficial to examine other potential predictors of delay, including SES, surgeon, treatment centre, whether or not patients were referred to another specialist after diagnosis, treatment type, and travel distance to treatment centre. Also not collected in the Registry were other important dates such as such as when the patient first detected a symptom of breast cancer, the first assessment by a physician and the first surgical consultation. As discussed earlier, there are a number of steps in the care pathway which could result in system delays. This study was only able to examine one of these intervals. Furthermore, there was no way to determine if some of the delay was attributable to the patient. It is possible that the patient contributed to longer delays by not accepting the diagnosis or missing appointments for treatment decision and surgery. This study assumes that the waiting times are only impacted by the system and its limitations. RHA boundary designation in Alberta is arbitrary, leading to difficulty explaining noted differences on a geographic basis. Finally, the large number of missing stage variables and the lack of quality control in assigning stages in the registry raises reliability questions regarding the interpretation of the results of stage. If an aggregate stage of TNM (tumor node

metastasis) components is not found in the chart, TNM components are identified and used to make the best estimate of stage by individual coders, not a pathologist. It is possible that some women are assigned an incorrect stage resulting in a misclassification bias.

This study also had various strengths. The source of the data, the Alberta Cancer Registry, has been tested and awarded the highest quality level by an independent evaluator (59). The data obtained allowed the examination of four consecutive years. Moreover, it was a population based study that captured 95% of breast cancer patients in Alberta each year. This made the study very powerful and afforded more generalizable results than other studies that have used samples from specific treatment centres and smaller time frames. It can also provide other provinces in Canada information on waiting time expectations and factors that contribute to longer delays.

5.5 Conclusions and Recommendations

The findings from this study have significant implications for health care delivery. Although there continues to be no data indicating the optimal time frame within which a woman should receive treatment, an expert group has recommended that no more than two weeks transpire between diagnosis and treatment. It is important to meet this target based on evidence that long delays can lead to advanced stage and reduced survival. It is true that this relationship is still under debate because of contradictory findings, however, it is understandable that women waiting for treatment of breast cancer are facing a tremendous

amount of anxiety. Thus, it is recommended that efforts have to be made to reduce the waiting times experienced by patients in Alberta because the data from this study indicate that there is a trend of increased delay rather than a decrease.

Questions of equal access to health services arise when centralization of health care services occurs, as it has in Alberta. The regional variation in waiting times between diagnosis and treatment established in this study suggests that patients from certain regions might have greater access to breast cancer services. Since this study began, the number of RHAs in Alberta has decreased from 17 to nine. Regardless of boundary designation, there is a significant difference in the waiting times of patients from Southern Alberta compared to those from Northern Alberta. These results should be disseminated to the RHAs and the Alberta Cancer Board for review. It is imperative that further examination of factors, including capacity, which could explain the significantly longer waiting times in the North, be conducted. Immediate implementation of solutions is important to ensure that some women are not inherently at a disadvantage because of where they live.

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