# DETERMINANTS OF WAITING TIME FROM INITIAL DIAGNOSTIC PROCEDURE TO SURGERY AMONG WOMEN WITH LOCALIZED BREAST CANCER IN QUEBEC, 1992-1997

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#### Abstract 1.

## Determinants of waiting time from initial diagnostic procedure to surgery among women with localized breast cancer in Quebec, 1992-1997

Background: The early diagnosis and treatment of breast cancer has become an important health care concern. A recent study reported the median waiting time for breast cancer surgery in Quebec was 34 days with 14% of women waiting in excess of 90 days. Understanding the determinants of long waiting is essential to develop optimum interventions to reduce delay. Objective: The purpose of this study was to identify the determinants of waiting time to surgery among women with primary breast cancer in Quebec between 1992 and 1997. Methods: The target population was all women 20 years and older diagnosed with primary breast cancer in Quebec between 1992 and 1997. The data was compiled from physician fee-for-service claims maintained by the Régie de l'assurance maladie du Québec (RAMQ); the Quebec hospital discharge database (MedEcho), and the 1991 Canadian census. Waiting time was defined as the number of days from the initial breast diagnostic procedure to the first definitive surgical treatment. Three-level hierarchical linear models were used for statistical analysis. Findings: Overall, 13,383 women with primary breast cancer treated by 614 surgeons in 107 hospitals were identified. No statistically significant variation of waiting time was found among hospitals. Longer waiting times for breast cancer surgery were observed for women 50 to 64 years of age, without comorbidity, with history of benign breast disease, living in the lower education areas, having surgery at day-surgery setting, having surgery in more

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recent years, or having surgery performed by younger a surgeon (20 to 49 years old). Women who had surgery performed in a teaching hospital had longer waiting times and this effect was larger when mastectomy was performed. These results could be used to identify women and care delivery practices at higher risk for delays which could be the focus of interventions.

For my parents, Rongjun Shen and Duofeng Liang

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#### Résumé 1.

Les déterminants du temps d'attente au Québec entre les procédures diagnostiques initiales et la chirurgie chez les femmes ayant un cancer du sein localisé, entre 1992 et 1997

Antécédents: Le diagnostic et le traitement précoce du cancer du sein est devenu un sujet de santé préoccupant. Une récente étude a rapporté que le temps d'attente médiant pour une chirugie pour le cancer du sein au Québec est de 34 jours et que 14% des femmes attendent plus de 90 jours. Il est essentiel de comprendre les déterminants de ce long temps d'attente afin de développer les interventions optimales pour réduire ce délai. Objectif: Le but de cette étude était d'identifier les déterminants du temps d'attente au Québec pour une chirurgie chez les femmes ayant un cancer du sein entre 1992 et 1997. Méthode: La population cible était toutes les femmes de 20 et plus qui ont eu un diagnostic de cancer du sein entre 1992 et 1997. Les données ont été compilées à partir des facturations pour les paiements à l'acte des médecins telles que conservées par la Régie de l'assurance maladie du Québec (RAMQ); la banque de données sur les hospitalisations (MedEcho), et le recensement canadien de 1991 de Statistique Canada. Le temps d'attente fut défini comme étant le nombre de jours entre la procédure initiale pour le diagnostic du cancer du sein et le premier traitement chirurgical définitif. Des modèles à trois niveaux hiérarchigues furent employés pour l'analyse statistique. Conclusions: Au total nous avons identifié 13 383 femmes avec le cancer du sein et 614 chirurgiens dans 107 hôpitaux. Il n'y avait pas de différence statistique pour le temps d'attente entre

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les hôpitaux. Les femmes âgées entre 50 et 64 ans ayant une ou plusieurs de ces caractéristiques: sans comorbidité, avec une histoire de cancer du sein bénin, vivant dans une région dont le niveau d'éducation est faible, qui ont eu une chirurgie d'un jour, qui ont eu une chirurgie dans les années les plus récentes ou qui ont eu une chirurgie pratiquée par un jeune chirurgien (20 à 49 ans), furent associées à une plus longue période d'attente pour une chirurgie pour le cancer du sein. Les femmes dont la chirurgie fut pratiqué dans un hôpital universitaire affilié ont eu un temps d'attente plus long et cet effet fut plus grand lorsqu'une masectomie fut pratiquée. Ces résultats pourraient être utilisés pour identifier des stratégies qui permettraient de réduire le temps d'attente pour un chirurgie pour le cancer du sein, par exemple, avec des programmes d'éducation et des changements organisationels.

#### Abstract 2.

## Prior Use of Mammography Protects against Late-Stage Breast Cancer: A Population Based View of Screening Effectiveness

**Background:** Randomized clinical trials provide evidence that screening mammography leads to a 30% reduction in mortality from breast cancer. The presumed mechanism for this protective effect is through detection of breast cancer at an earlier stage. The purpose of this study is to estimate in the general population the impact of prior mammography on the stage of presentation of breast cancer. Method: Records of physician fee-for-service claims and hospitalizations were obtained for all Quebec women 20 years of age and over who had a diagnosis of breast cancer between 1992 and 1997. Tumours diagnosed as primary breast cancer with positive lymphatic nodes or with a disseminated cancer were classified as "late-stage". Prior mammography was defined as having at least one bilateral mammogram in the 30-month period before the episode of breast cancer care. Results: Among the 23,216 women diagnosed with breast cancer, 29% were classified as having a diagnosis of latestage breast cancer. On average, 13.7% of women with breast cancer had a mammogram during two and a half years before their episode of care for breast cancer. The authors found a 39% relative reduction in late-stage breast cancer among women 50 to 69 years of age, and a 58% relative reduction in women age 70 years and older. **Conclusion:** Regular use of mammography was associated with a higher probability of detecting breast cancer at an earlier stage, in agreement with data from randomized clinical trials. Evidence is added to support the development and maintenance of organized screening programs.

#### Résumé 2.

La mammographie préventive protège contre la détection du cancer du sein à un stade avancé: une étude sur l'efficacité du dépistage vue sur une base populationelle

Antécédents: Les essais cliniques randomisés fournissent des preuves que le dépistage par mammographie conduit à une réduction de 30% de la mortalité due au cancer du sein. Le mécanisme présumé de cet effet protecteur vient de la détection du cancer du sein à un stade primaire. Objectif: Le but de cette étude est d'estimer l'impact de la mammographie préventive dans la population générale, sur le stade du cancer du sein à sa détection. Méthode: Les données sur les paiements à l'acte des médecins et sur les hospitalisations furent obtenues pour toutes les femmes du Québec âgées de plus de 20 ans et qui ont eu un diagnostic de cancer du sein entre 1992 et 1997. Les tumeurs diagnostiquées comme étant un cancer du sein avec ganglions lymphatiques ou avec dissémination furent classifiées comme étant un stade avancé. La mammographie préventive fut définie comme étant une mammographie bilatérale subie 30 mois avant l'épisode de soins pour un cancer du sein. **Conclusions:** Parmis les 23 216 femmes qui ont eu un diagnostic de cancer du sein, 29% furent classifiées comme ayant un cancer du sein à un stade avancé. En moyenne, 13,7% des femmes avec un cancer du sein ont eu une mammographie au cours des deux années et demi avant leur épisode de soins pour le cancer du sein. Les auteurs ont trouvé une réduction relative du stade avancé du cancer du sein de 39% chez les femmes de 50 à 69 ans, et de 58%

chez les femmes de 70 ans et plus. En conclusion, nous avons trouvé que des examens mammographiques réguliers étaient associés à une probabilité plus élevée de détecter un cancer du sein à un stade primaire, ce qui est en accord avec les données des essais randomisés. Ces évidences viennent supporter le développement et le maintien de la planification de programmes de dépistage.

#### PREFACE OF THESIS

#### **Description of Thesis**

The structure of this thesis is the manuscript-based thesis, which is supported by the McGill University Faculty of Graduate Studies and Research regulations for the "Guidelines Concerning Thesis Preparation". The format of the manuscriptbased thesis requires that the paper should have a cohesive, unitary character and a report of a single program of research.

The thesis contains 6 chapters. The first chapter is the introduction to the research question, rationale of study and research objectives. The second chapter is the review of the literature and the justification and rationale for the research questions. The third, the fourth, and the fifth chapters are three manuscripts written in a format suitable for publication in a scientific journal. Each of the three articles is linked by a preface. Each manuscript is written to be an individual document which addresses one or more of the objectives of the research project. There will be necessarily overlap and repetition in the methods of the study. The sixth chapter is conclusion, concluding a summarizing of the results and the discussion of the implications for research and practice.

Tables and figures with a prefix, which corresponds to the sections, are included at the end of each section or article. The references are listed at the end of thesis for all sections of the thesis. Appendixes contain an overview of the research methods, which provides more detail than would be appropriate for a manuscript regarding the data source and data management, variable definition and measurement, and statistical analysis.

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### Authorship

Since this project is part of the larger research project of waiting time for breast cancer surgery in Quebec (Mayo et al, 2000), some of the co-variates such as waiting time and episode of care, were common and were jointly defined and used. The variables specific to this research were defined entirely by the candidate. A number of people contributed to this study, and their contributions are gratefully acknowledged. The candidate functioned as principal investigator in all aspects of study design, operationlization of study variables, statistical analysis, interpretation of findings and writing of the manuscripts. Three manuscripts are co-authored with members of the candidate's Thesis Supervisory Committee. Through the entire project they advised on the design, analysis, and presentation of results. Co-author Susan Scott was not on the thesis advisory committee, but she contributed significantly to initial data management, interpretation of results and review of drafts. The candidate would be responsible for the scientific quality of the research, the originality of the ideas, the accuracy of the data and quality of reporting.

#### Originality

To the candidate's knowledge, this is the first research which attempts to identify the determinants of waiting time from initial diagnostic procedure to the first definitive surgery for women with breast cancer. This period of waiting time was defined as "provider delay" in the literature and the factors influencing provider delay have not been well reported. It is the first time the determinants of waiting time to surgery using medical administrative databases in Quebec. This is a very efficient data source for health care service research, covering all women with breast cancer in the study province.

This research study contributes to the methodology for health care research by using hierarchical modelling strategy which is relatively new in the application of epidemiological data. To the candidate's knowledge, it is the first time this methodology in the study of the determinants or waiting time and the determinants of pattern of care for women with breast cancer at patient-, physician-, and hospital-level. Hierarchical modelling corrects the biased estimates of the association as ignoring cluster effects by conventional regression model.

This research contribute to the knowledge of the pattern of care for women with breast cancer, by investigating the variation and the determinants of the type of diagnostic procedure women went through, number of procedure before surgery and the type of surgery selected. It adds evidence of variation pattern for selection of type of surgery, but the study of pattern of diagnostic procedure has not been expressly studied before. This research also contributes to add supportive evidence of beneficial effect of screening mammography using population-based study. Given no organized provincial screening mammography program in Quebec between 1992 and 1997, this study provides such information at the provincial basis during this period.

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#### Acknowledgements

This project could not have been accomplished without the contribution and support of many people. First of all, it has been a great honour to have Dr. Nancy Mayo as my thesis supervisor. This particular project is one part of a larger study of waiting time for breast cancer surgery for which Dr. Mayo is the principal investigator. She provided the essential material and allowed me full access to resources in her research laboratory, where she always provides a flourishing learning environment for her graduate students. Nancy's special research talent, her encouragement, her clear-minded guidance, and her kindly care have been an important support throughout all the period of this project and will influence me in my future professional life.

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I would like to express special thanks to Dr. Timo Partanen, my Finnish supervisor. Without his sweet encouragement and kindly reference, I would not have met Nancy and Mark, and I would not have started my endeavour to PhD. I am indebted to Dr. Judith Singer from Harvard University who cheerily answered my e-mail questions about hierarchical modelling.

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### Chapter 1. Introduction

#### Background

The importance of an early diagnosis of breast cancer has been widely emphasised. Both Health Canada and the Canadian Medical Association have recently proposed clinical practice guidelines for the care and treatment of breast cancer that stress a timely work-up and diagnosis. Within the guidelines, it is frequently cited that "The detection of a breast lump is a source of great anxiety to a patient until its nature is determined. To diminish the psychological stress caused by diagnostic uncertainty, the work-up of a breast lump should be completed as rapidly as possible and long waits to obtain tests should be avoided."<sup>1</sup> Health education programs for women that incorporate screening mammography, clinical breast examination and regular self-breast examination are the principal means of early detection of breast cancer. However, early diagnosis is effective only if the needed treatment can be delivered in a timely fashion. Treatment delay is not only difficult for the patient, but it can affect outcome, particularly in a potentially curable cancer, such as breast cancer.

Canada provides universal health insurance coverage for its population through health insurance programs jointly financed by federal, provincial and territorial authorities. Provincial and territorial authorities design their own health insurance programs following the criteria outlined in the Canada Health Act applying to the

following: public administration, comprehensiveness, universality, portability, and accessibility <sup>2</sup>.

A feature of a universal health care system is the attempt to offer the same health care services to everyone on the basis of need rather than the ability to pay. Universal health care, as currently provided for Canadians, has succeeded in bringing about a high degree of equality to access of hospital and medical services. Nevertheless, problems of accessibility continue to exist and rapid access to the health care system for necessary treatment is sometimes impossible.

Accessibility to the services of the acute-care hospital is coming under increased public scrutiny. Treatment delays, waiting lists, bed closures and shortages of health care professionals are specific problems associated with access to care, in particular acute care and high technology procedures<sup>3</sup>.

Studies describing the natural history of breast cancer, based on evidence from screening programmes, have suggested that breast cancer does indeed behave as a progressive disease. The time of diagnosis and treatment is extremely important in determining outcome<sup>4</sup>. Richards et al.<sup>5</sup> in their systematic review on the influence of delay on survival in patients with breast cancer indicated that "Patients with delays of 3 months or more had 12% lower 5-year survival than those with shorter delays (OR death: 1.47; 95% CI: 1.42-1.53). These effects cannot be accounted for by lead-time bias. Efforts should be made to keep delays by patients and providers to a minimum."

The Quebec government has recently released an action plan for eliminating delays in surgery in this province<sup>6</sup>. However, aspects concerning the situation of waiting time for breast cancer surgery in Quebec are unknown. The determinants of long waiting time for breast cancer surgery have not been studied. Successful identification of the factors associated with long waiting time could lead to diminished delays in diagnosis and treatment procedures in the Quebec province by interventions directed at where they are most needed. Consequently, shorter waits may have a positive impact on survival as well as the psychological well being and quality of life of women living with the experience of breast cancer.

Knowledge of the scope and determinants of unexpected long waiting time in the diagnosis and treatment of breast cancer is limited. Delay can be considered as two components, patient delay and system delay. Patient delay is the interval between first discovering a breast symptom and the initial presentation to a health professional. System delay is the time it takes for a woman to be diagnosed and treated once she has entered into the health care system. In fact, when we examine the factors influencing waiting time, it is impossible to completely separate patient delay from provider delay. Patients may indeed contribute to delays that occur after provider consultation. For the purpose of studying predictors of waiting time for diagnosis and treatment after women enter the system, individual characteristics need to be considered.

In most reports, prolonged delays are usually defined as intervals greater than three months. Such delays have been shown to be associated with increased

tumour size <sup>7-10</sup>, more advanced stages of breast cancer<sup>10-14</sup>, and with worse long-term survival<sup>15</sup>.

This thesis is a sub-component of a larger study led by Dr. Nancy Mayo, which was funded by National Cancer Institute of Canada (NCIC) (Project # 008020). The main study described the waiting time for breast cancer surgery in Quebec from Jan. 1, 1992 to Dec. 31, 1998. The main study included women aged 20 or more who underwent an invasive procedure for the diagnosis or treatment of breast cancer in the index period from January 1, 1992 to December 31,1998. After completion of analysis for this thesis, data came from the RAMQ for information of 1998 was added to the main study, but could not be incorporated in the thesis analysis. The results of the main study showed half of the population had to wait six weeks. Waiting time increased over time and the median waiting time was 28 days in 1992 but 42 days in 1998. About 15% of women who underwent surgery had to wait more than three months from initial diagnostic procedures before surgery was a determinant of waiting time.

Thus, in this thesis, the first action was to identify determinants of pattern of care, including type of procedure and number of procedures, before going on to examine the determinants of waiting time as the variables are inter-dependent. As the process of care for breast cancer including women, physicians, and hospitals, the statistical analysis needed to consider the variables at all three levels. Hierarchical models were applied to resolve statistical issues involving nested hierarchical data structures and to account for the clustering effects in this study.

The purpose of the present study is to identify the determinants of long time interval from the initial procedure to surgical treatment of breast cancer. Successfully determining the factors associated with long system waiting would make it possible to direct interventions where they are most needed. In order to provide information for potential interventions at patient, physician or institutional levels, the three levels of predictors will be determined simultaneously by taking cluster effect into account. The chapters to follow will consist of a literature review describing the epidemiology of breast cancer, treatment options, diagnosis and treatment delays, the impact of delay, and the potential predictors of delay. Subsequent chapters include three manuscripts from the study, methodological issues, and conclusions. An overall view of study design and data management will be attached to the appendix.

#### Objectives

The overall purposes of this study were:

- To identify determinants of waiting time from the initial breast diagnostic procedure to the first surgical treatment for women with primary breast cancer in Quebec between 1992 and 1997. To identify hospital, the physician, and individual determinants of waiting time.
- To describe the pattern of care, including type of surgery, type of diagnostic procedures, and number of procedures, for women with breast cancer in Quebec between 1992 and 1997, and to identify factors contributing to the variation in pattern of care.

- 3. To estimate in the general population the impact of the prior utilization of mammography within 2 years before the episode of breast cancer care on the stage of presentation of breast cancer.
- 4. To compare the results of multilevel models with those of conventional linear models or logistic models, and validating these models by analysis of simulated data.

### **Chapter 2. Literature Review**

#### 2.1 Breast Cancer Prevention and Control

2.1.1 Epidemiology of Breast Cancer: Incidence and mortality

Breast cancer is the most common cancer in Canadian women, accounting for about 30% annually of all new cancers. An estimated 18,700 cases were diagnosed in Canada in 1999<sup>16</sup>. Breast cancer incidence has risen steadily during the past decade. The incidence of breast cancer increased from 84.8 in 1980 to 112.5 (per 100,000 women) in 1998 in United States<sup>17</sup>, and from 90 in 1984 to about 100 in 1994 in Canada<sup>18</sup>. This is due, in part, to increased effectiveness of detection because of the rising number of mammography examinations since the mid-1980s.

In 1999, the number of deaths from breast cancer was estimated as 5,400 women<sup>16</sup>. According to the 1997 Canadian Cancer Statistics, breast cancer mortality rates have declined slightly since 1985 and particularly since 1990. The age-standardized mortality rate for breast cancer (per 100,000 woman-year) was 31.7 in 1985 and 28.8 in 1997<sup>16</sup>. The decline in mortality of breast cancer observed in Canada has been attributed to both earlier detection by screening mammography and improvement of technology of the treatment<sup>19</sup>. Although age-standardized mortality ratios have fallen slightly in the past decade, breast cancer is currently the leading cause of death among women between the ages of 35 and 55 in North America.

Breast cancer is a major health problem in Quebec with significant social and economic impact on the population and on the health care system as well. In 1987, breast cancer accounted for 26% of all new cases of cancer diagnosed in Quebec women<sup>20</sup>. Each year nearly 4,000 new cases are reported and approximately 1,200 women die from this disease annually in Quebec<sup>21</sup>.

Most of the established risk factors for breast cancer contribute rather modest elevations in risk, and few are readily modifiable by either changing of environmental factors or changes in behaviours<sup>22</sup>. Primary prevention of the occurrence of the disease process of breast cancer is not yet possible. This is primarily because most of the identified risk factors do not increase risk greatly and, secondly, because many of the risk factors, such as age and family history, are not modifiable. Secondary prevention of breast cancer, through mammography screening and tertiary prevention of mortality, would be the promising means of reducing the impact of breast cancer. Early detection and treatment give the best opportunity to reduce mortality. Therefore, efforts to promote early detection and treatment are the major focus on fighting breast cancer.

#### 2.1.2 Clinical Features and Stages

Even though most breast lumps are benign, all breast lumps should be regarded as potentially malignant and a firm histological diagnosis is always necessary<sup>23</sup>. Pain in the breast, discharge or bleeding from the nipple, and pain or swelling in the axilla, should also be investigated.

Almost all breast cancers are called adenocarcinomas, which means these cancers arise from the glandular parts of the breast. Depending on the histology, Northridge et al. found that infiltrating duct carcinoma accounted for about 68% of female breast cancer<sup>24</sup>. In recent years, there has been a steady increase in the proportion of cancer cases diagnosed as ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). Although DCIS and LCIS are recognized as early lesions, there may be widespread abnormalities within the breast which suggests that these may need to be considered as a separate type of cancer<sup>7</sup>.

Since the beginning of the century, there have been many attempts to provide a simple staging system to describe the degree of advancement of the tumour<sup>25-27</sup>. The TNM staging system has become widely accepted for its precision in tumour stage classification. TNM classifies the primary tumour into four stages based on the size of tumor (T), the presence of clinically abnormal axillary nodes (N) and distant metastatic disease (M)<sup>26,27</sup>.

2.1.3 Practice Guidelines for Diagnosis and Treatment of Breast Cancer

To facilitate the interdisciplinary care for breast cancer, Health Canada and the Canadian Medical Association published a Canadian consensus document: Clinical practice guidelines for the procedures of breast cancer diagnosis and treatment<sup>1</sup>.

#### Screening Mammography

The guidelines from Quebec as well as those from most other Canadian provinces recommend a screening mammography every 1 to 2 years for all Canadian women from 50 to 69 years. Screening for women aged 40 to 49 years is recommended only for those who are at high risk of breast cancer. Women defined as high risk are those with biopsy-proven benign breast disease and those with a first-degree family history of breast cancer<sup>21,28</sup>. Approximately 333,100 women receive a mammography each year in Quebec<sup>21</sup>.

Screening mammography offers several benefits. These benefits include a demonstrated decrease in mortality for women older than 50 years, the ability to use conservative surgery for smaller, less advanced lesions, and the psychological release gained by a normal mammogram<sup>29</sup>. However, there is about a 15% false negative result in women over 50 years, and a 20-30% false negative result in women younger than 50 years<sup>30</sup>. A false negative mammogram result could be hazardous if the woman delays seeking appropriate care when she subsequently notices a breast lump. False negative mammogram results can lead to an increased delay for diagnosis and treatment.

Conversely, false positive mammography reports would increase the burden for both women and the health care system. Elmore et al.<sup>31</sup> estimated the cumulative risk of a false positive result for the women who participated in the Screening Mammography of British Columbia (SMPBC). Of the 9,762 women who were screened, 23.8% had at least one false positive mammogram. Among women without breast cancer, an estimated 18.6% (9.8-41.2%) underwent a biopsy after 10 mammograms. Although there have been some suggestions that the

cumulative risk of false positive might be overestimated by Elmore.<sup>32</sup>, previous studies have reported similarly high false positive results <sup>29,33</sup>. As the use of mammography screening increases, more abnormalities will be detected in healthy women leading to increased anxiety and decreased quality of life for the women, their families, as well as burden the health care system for follow-up<sup>34,35</sup>.

#### Confirmation of diagnosis

Although most lumps detected in the breast are benign, it is necessary to further confirm the pathology once a lump or suspicious breast symptom is discovered. Figure 2.1 shows the confirmation diagnosis pathway for a woman with suspicion of breast cancer. The process of confirmation includes investigating whether there is a history of breast biopsy or breast cancer, doing a physical examination and performing a mammography or ultrasonography. Whenever reasonable suspicion of a tumour remains, an aspiration or needle biopsy, core needle biopsy, or an excisional biopsy should be carried out<sup>1</sup>.

#### Management of the breast cancer

The recommended treatment pathway after breast cancer has been diagnosed is showed in Figure 2.2. For patients with earlier stages of breast cancer (stage I and II), breast-conserving surgery (lumpectomy or wide local excision) followed by radiotherapy is most recommended. Other options of surgical treatment are simple mastectomy, modified radical mastectomy and radical mastectomy. The choice of treatment will depend on tumour size and type, age and health status of the patient, and physician and patient preference of treatment<sup>1</sup>.

Currently, breast cancer with distant metastasis is not curable. Therefore, the main aim in the management of locally advanced and disseminated breast cancer is palliation. Of the variety of palliative treatments available, hormonal therapy and chemotherapy are the two most preferred<sup>36</sup>. Summary of literature review for the pattern of care is shown in Table 2.6.

#### 2.2 Waiting Time and Delay

The operational definitions of delay remain largely arbitrary. Of course there is always some waiting time between procedures. The question is what is the actual time delay and what is an acceptable time interval. Most of the relevant studies have used the term 'delay' with a negative connotation implying that any time elapsed between procedures would result in a harmful outcome. This may not necessarily be the case as both the patient and the physician need time to make a decision.

#### 2.2.1 Patient delay

Patient delay is generally defined as the time interval between the onset of the initial breast symptoms and the first consultation for medical services. In their review of 12 studies of patient delay, Facione et al.<sup>37</sup> found that 34% of women with breast cancer symptoms delayed seeking help for three or more months. Delay appeared to be a conscious and deliberate act performed by many patients with awareness of their symptoms of breast cancer<sup>38</sup>.

Studies reporting the extent of patient delay are summarised in Table 2.1. The operational definition of delay was largely arbitrary. In all studies, the self-
discovery of symptoms defined the beginning of the time period and the end point was defined by various events including the first medical consultation, biopsy, diagnosis, or first treatment. Most of studies defined delay as a time period of greater than three months from the initiating breast symptoms to the first presentation to a physician. About 31% out of 28,940 patients in these studies delayed consultation. Rather than judge the appropriateness of the delay or norms for waiting, most investigators have described only the prevalence of delay. All studies were retrospective and their validity was threatened by potential recall biases. Although one might suspect that women with breast symptoms may be overestimating or underestimating the symptom duration, some researchers have observed that women were quite accurate in marking the time when their breast symptoms started<sup>39-41</sup>.

#### 2.2.2 System delay

Although patient delay has been studied extensively<sup>38,42</sup>, there has been little research on system delay for breast cancer diagnosis and treatment<sup>12,43-45</sup>. System delay is defined as the waiting time for a woman to be evaluated, diagnosed, and treated once she has had a consultation with a physician or she has had a finding of an abnormal mammography. Studies related to system delay are presented in Table 2.2.

More than 20 years ago, it was suggested that health services for breast cancer patients could be improved by more effective education of both patients and doctors, and by a more structured system of care<sup>46</sup>. However, system delays

continue to be demonstrated across countries. In a study of 367 American women, Caplan et al. {1996} found that about 45% experienced health care system delay for three months. Similar results were seen in British studies<sup>47,48</sup>. Researchers from the GIVIO centre in Italy performed an examination of the diagnostic processes of 1110 newly diagnosed women and found that 36% were diagnosed more than three months before proceeding to treatment<sup>8</sup>. About 24% of women waited 2 weeks for confirmation of the diagnosis and in an Australian study, 12% waited more than 4 weeks<sup>49</sup>. In contrast, Gould-Martin et al.<sup>12</sup> found no evidence for increased delay after the initial physician visit in States.

Researchers examined waiting time for radiotherapy in Ontario. They reported a median waiting time of 59 days from surgery to initiation of radiotherapy for the 4,971 women diagnosed with breast cancer in 1990. There was a marked increase in waiting time between 1982 and 1991. They also found that waiting times for radiotherapy after surgery for other cancers was considerably longer in Ontario than in the USA<sup>50,51</sup>. However, a study comparing Washington State, USA and British Columbia, Canada found that the median delay from first symptom to definitive treatment was similar in the two regions<sup>52</sup>.

In the most recent study, the Manitoba Centre for Health Policy and Evaluation studied waiting times from 1992 to 1996 for eight non-emergency surgical procedures including breast operations<sup>53</sup>. The waiting time for excision of breast lesions was consistent at a median of 16 days, and they concluded that the median waiting time was stable during this time period. The waiting period in the Manitoba study, however, was defined as the time from the last visit to the

surgeon to surgery. This definition would therefore ignore multiple preoperative visits and this may not be reasonable.

The Fraser Institute in British Columbia conducted a national survey, based on physician self-report concerning the length of time a new patient could expect to wait for treatment, from GP referral to specialist visit, and from specialist visit to treatment. The study reported that, in general, Canadians are waiting longer, with an increase in overall waiting time by 9% between 1996 and 1997<sup>54</sup>.

Benk et al.<sup>55</sup> studied 739 patients with Stage I and Stage II breast cancer who were treated with conservative surgery at three McGill University hospitals from 1992 to 1993. Using the interval from the date of surgery to the date of the initial radiotherapy treatment, they defined delay as waiting more than 7 weeks for women who did not receive chemotherapy, and more than 24 weeks for those who received chemotherapy. Based on this definition, they found that more than half of the patients were delayed for radiotherapy.

Studies of waiting time for surgical procedures including CABG<sup>56-60</sup>, heart transplant <sup>61,62</sup>, orthopaedic surgery<sup>63</sup> and gynaecological surgery<sup>64,65</sup>, have been conducted over the past few years. Based on evidence of lengthy waiting times for these surgical procedures, the Quebec government has released an action plan for eliminating delays for surgery. This plan raises the question of long waiting time in Quebec relative to other areas in North America<sup>6</sup>. Although breast cancer surgery is the fourth most common surgery in Quebec<sup>66</sup>, there are no data on the waiting time for breast cancer surgery in this province. Further, there are no

studies on the determinants of waiting time. Thus, a study on waiting time for breast cancer surgery and its determinants would provide important information for decision-makers in improving the quality of health care for this population.

#### 2.3 The impact of long waiting time (delay)

#### 2.3.1 Stress and anxiety

Waiting for potentially life-threatening news can have negative psychological consequences. Investigators have reported that distress is highest around the time waiting for diagnosis<sup>67-70</sup>. Many patients have experienced anxiety provoked by suspicious mammography findings<sup>71,72</sup>. As long delay for the final diagnosis may increase stress, it is of critical important to obtain the final diagnosis in a timely manner.

The consequences of increased waiting times are not only psychological but may also worsen the overall outcome of the disease by impacting on tumour growth, recurrence, and survival. Experimental animal models provide biological evidence in support of this hypothesis.

By using female mice of the C3H/He strain carrying the Bittner oncogenic virus, Riley<sup>73</sup> observed that 92% of female mice under chronic stress developed mammary tumours compared with only 7% in a protected environment. He suggested that stress may have increased their risk of mammary carcinoma by influencing their immunological tumour surveillance system. Using the same animal model, Visintainer<sup>74</sup> also reported that lack of control over stressors

increased tumour incidence. Stress and coping factors resulted in exaggeration of tumour size and decreased survival time in rats<sup>75,76</sup>. To explain this phenomena, a laboratory model of stress enhancing tumour growth was reported<sup>77</sup>,

stress --> decrease cytotoxic activity of natural killer (NK) cells

decrease immune function ----- decrease surveillance against tumours

By a similar mechanism, stress may significantly increase tumour metastases<sup>78,79</sup>. These animal models may be applicable to humans. If similar relationships among stress, immune function, and metastasis occur in humans, decreasing the stress women experience during diagnosis and treatment may impact on recurrence and survival. Reducing waiting time, which will diminish stress and anxiety, should be considered as an important component of the breast cancer care.

2.3.2 Recurrence of breast cancer

A study of the effect of delay of post-surgery radiotherapy on local breast cancer recurrence was carried out in McGill University hospitals. After partial mastectomy for early stage breast cancer in 486 patients, the risk of 5-year local recurrence of breast cancer was 5 times higher for women who waited over 79 days for radiotherapy<sup>55</sup>. Although waiting for radiotherapy was found to increase recurrence, an earlier study found no relationship between physician delay and breast cancer recurrence<sup>80</sup>. These results may be biased as potential confounders, such as patient's age and the stage of the tumour were not

controlled. Therefore, the evidence of impact of delay on recurrence of breast cancer is presently insufficient.

2.3.3 Quality of Life

A recent study demonstrated that a false positive mammogram significantly affected the woman's quality of life<sup>34</sup>. The greatest impact of waiting time was on general health, physical function and social function. Thus, it is of utmost importance that waiting time for confirmatory diagnosis is kept to a minimum. Better quality of life will result from treating early breast tumours with lumpectomy rather than radical mastectomy <sup>81</sup>. A lumpectomy is a less incapacitating procedure and leads to better cosmetic results. The factor which most influences the type of surgical procedure performed is the extent of spread of the cancer at the time of surgery<sup>82</sup>. This supports the idea, therefore, that breast cancers should be detected and treated as early as possible.

#### 2.3.4 Survival

Most studies have reported that diagnostic delays of 3-6 months and a more advanced stage of cancer at the time of diagnosis increase mortality<sup>14,83-91</sup>. Although the results of several studies suggested that the possibility of cure was confined mostly to the earliest stages<sup>36,92-95</sup>, other studies demonstrated no such association<sup>80,96-98</sup>. Sainsbury<sup>99</sup> found that patients who presented to the system early and were treated in less than 30 days had significantly worse outcomes. Furthermore, Neave<sup>9</sup>, in a study of 1675 breast cancer patients in Auckland, reported that short delay was associated with an advanced grade of tumor and

poorer survival. These findings, however, may reflect rapid growth or change in the size of a lump that may lead the woman to present early and be treated quickly. These tumours may in fact be the most aggressive phenotypes with metastases already occurring during the pre-clinical phase.

Richards et al.<sup>5</sup> reviewed 87 studies with 101,954 patients. Cut-off points for delay of 3 months and 6 months were chosen based on the most frequently reported times in individual reports. Sixty studies (71.3%) supported the primary hypothesis that longer delays were associated with worse survival rates. In those studies that did not support the hypothesis, the sample sizes were usually smaller on restricted samples, including only certain stages of breast tumours.

A study of 160 women with breast cancer demonstrated that a decrease in the time for diagnosis and treatment could favourably influence survival for patients with non-aggressive tumours. For those with fast-growing tumours, early diagnosis and treatment during the symptomatic period is unlikely to alter their chances for better survival. For these patients, to improve their prognosis, efforts should be focused on the detection of asymptomatic cancer<sup>100</sup>.

Treatment delay also decreases the probability of eradication of the tumour by radiation, and increases the distant metastasis outside the treatment field. Table 3 shows the impact of provider delay on breast cancer outcomes. From 30 studies identified in this review, 73% of studies support the hypotheses that long delay will significantly decrease survival, 20% showed no effect of delay, and only two

studies failed to support the hypotheses. Prompt access to treatment in this situation is, therefore, an important aspect of survival and quality of care.

The conflicting study results concerning survival may reflect methodological issues, including various definitions of 'delay', lack of control of potential confounders. Lead-time bias exists when the survival period is measured from the date of diagnosis. If diagnosis is delayed, the remaining time to death is relatively shorter. Some studies took lead-time bias into account<sup>11,96</sup>, while others did not. Confounding by indication may be the other major bias when studying the association between delay and survival. Such bias arises if rapid progression of the tumour leads the patient to seek help promptly, and physicians to make decision quickly. Shorter delays would therefore be associated with poorer survival because of the aggressive nature of the tumours. Earlier studies showed that the failure to detect the expected inverse relationship between delay and survival was largely due to confounding by histology grade or the inherent malignancy of the cancers. When such confounding by indication was removed, delay was strongly associated with reduced survival<sup>83,101</sup>.

In summary, studies of the consequences of delay on breast cancer prognosis tend to support, after adjusting for disease severity, that increased diagnostic delay is associated with more advanced stage of cancer at diagnosis, and subsequent worse survival (Table 2.3). Detection and treatment of cancer at an early stage would improve the prospects for long-term survival for most biological types of breast cancer. Total waiting times should be kept to a minimum for a better prognosis.

#### 2.4 Predictors of the waiting times

The purpose of the study is to examine the time interval between a series of diagnostic and treatment procedures after a woman has entered the health care system. It is a study of system delay, which as previously defined, may include both physician and hospital delay. We assume that women themselves may also contribute to the delays that occur after the initial physician consultation. Therefore, for the purpose of identifying the predictors of long waiting time, both patient and system related factors are important. In the following section, studies investigating determinants of both patient and system delay will be reviewed.

#### 2.4.1 Patient Delay

Risk factors for patient delay that have previously been examined can be classified into three main categories: i) sociodemographic factors including age, marital status, socio-economic status and race; ii) clinical factors including the nature of the first symptom, comorbidity and a history of breast disease; iii) psychosocial factors. Information concerning predictors of patient delay is summarized in table 2.4.

#### <u>Age</u>

A majority of studies have supported the hypothesis that older age is associated with longer patient delay<sup>15,46,47,102,103</sup>. Both a recent<sup>104</sup> and a past review<sup>105</sup> reported a consensus that older women significantly delayed help seeking. There are several underlining hypotheses. Older women may lack current information

about breast cancer therapy and prognosis. Contributing their symptoms of illness to normal aging also may lead older women to delay their first consultation for breast symptoms<sup>106,107</sup>. A higher incidence of competing comorbidities and disabilities has also been hypothesized to contribute to the delay. Despite this studies did find influence several not age to patient support. delay<sup>10,12,45,48,106,108,109</sup>. It may also be that older patients have difficulties in making treatment decisions, may be less likely to attend their appointments even after entering the health care system, and therefore, more likely to have longer intervals between breast procedures.

#### Socioeconomic Status

#### 1. Marriage

In their review of factors predicting delayed presentation of symptomatic breast cancer, Ramirez et al.<sup>104</sup> cited eight studies that demonstrated no association between marital status and patient delay. Two further studies found no difference in the time to seek a medical consult between married and widowed women<sup>101,110</sup>. Williams et al.<sup>47</sup> found that married women with children were more like to have a delay of greater than three months than single women. Among the women who delayed in this study, 3% claimed that they had delayed for family reasons.

#### 2. Education

Education level and its potential role with patient delay has been examined in several studies. Most studies reported a longer patient delay among the less

educated<sup>105,111,112</sup>. Williams<sup>47</sup> found education level to be significant only in the early delay, as women with college level education or greater were less likely to delay one month than those with primary or secondary school education. But the categorization of educational levels was inconsistent and often categories were not mutually exclusive. In contrast, several other studies did not find an effect of education level on patient delay<sup>8,106,113</sup>.

#### 3. Income

Gold-Martin et al.<sup>12</sup> found, in a sample of women with breast cancer, that those with lower socioeconomic status (SES), as measured from census information, delayed twice as long as women of higher SES. Hackett et al.<sup>38</sup> used a two-factor index of social position, which included both occupation and education, to demonstrate that those in lower SES groups tended to delay longer than those in higher SES groups. However, Hackett's work indicated the role of social position on the amount that people worry about their health. The lower the social class, the more people tended to delay. It is likely that worry about expand might influence the delay. Antonvosky et al.<sup>105</sup> in their review of literature found lower SES to be consistently associated with patient delay. The reasons for this finding might be that patients of lower SES know much less about their illness than those in the higher class. This association with SES may also reflect an unequal access to health care for the two groups or less personal and natural resources to negotiate their way through a complex health care system. Those in a higher SES group are perhaps more likely to have a stable and continuous source of care through their primary physicians.

In Canada, Battistella<sup>44</sup> In a study of 210 Canadians, aged 45 and older by using data from a 1971 population survey found no evidence of lower SES increasing delay. One recent British study also found no significant association between SES and patient delay<sup>48</sup>.

From this review, there is support that the effect of socioeconomic status on patient delay for diagnosis of breast cancer may depend upon the type of health care system. In systems where individuals pay their private health care insurance or pay their health care fees (American system), those with limited financial resources may have difficulty accessing the health care system, thus leading to increased patient delay. However, where individuals are covered by a universal health insurance, such as Canadian health care system, the impact of income should not be as strong.

#### <u>Race</u>

Non-whites have been found to have poorer survival rates even when age and the stage of breast tumour are taken into account<sup>84,112,114</sup>. One reason for the better survival in white people is that whites, on average, seek medical care at an earlier stage than do non-whites<sup>114-117</sup>. Previous researches on health care utilization in minority American populations indicate that African Americans utilize health care services less, regardless of their degree of illness<sup>118-120</sup>. Dennis<sup>80</sup> found, among 237 breast cancer patients in Brooklyn, no association between race and patient delay. However, these studies did not control for important confounders, such as age, socioeconomic status, and particular health knowledge.

#### **Clinical factors**

#### 1) History of benign breast diseases

A woman's past experience with breast symptoms may be a determinant of delay in either a positive or a negative way. One might assume that a history of benign disease may cause women to believe that current breast symptoms are caused by previous breast disease and thus, they may be more likely to delay seeking professional help. Gould-Martin and co-workers' study<sup>12</sup> supports an association between a personal history of benign breast disease and longer patient delay. Women with a history of benign disease had a median delay of 13.5 days compared with 7 days in women without such a history. Adam<sup>45</sup> found the same delay with women assuming the previous benign breast disease to be the cause of their current lumps. On the other hand, one could speculate that the past experience of breast disease would be associated with a shorter delay, as women are alerted to their higher risk of breast cancer.

#### 2) Nature of the symptom

The nature of the breast symptom has been reported as an important factor to influence the timing of seeking help. Some studies found that patient delay for benign disease was shorter than for malignant tumour<sup>102,110,121</sup>. In their review of the literature, Ramirez et al.<sup>104</sup> reported that discovery of breast symptoms other than a lump is a moderate risk factor for the patient delay. A lump, with or without accompanying pain, was the most common presenting symptom, occurring in 65% to 86% of all cases<sup>10,12,40,45,48,85,102,115,122</sup>. Two other studies observed no difference

in delay by presenting symptoms<sup>113,123</sup>. Their small samples may have contributed to their negative findings.

3) Health status and comorbidity

Whether a woman with one or more chronic illnesses is more or less likely to seek help early for a breast cancer symptom has not been examined frequently. Safer<sup>43</sup> reported that patients who did not have a competing health problem were less likely to delay seeking care for their painful breast symptom. One could assume that persons with comorbidities would have a habit of utilizing the health care system and an established relationship with their health care providers and thus, be less likely to have long patient delay. However, one could also argue that factors like the symptoms of other conditions may mask the symptoms of the new breast disease. In a health care system that is not publicly funded, a reluctance for a patient to spend more money on health care might contribute to a longer patient delay. More studies are needed to test these hypotheses. By using the hospital discharge database, we will have all the information about the principal and the secondary diagnosis for each admission. A comorbidity index can be created to test the hypothesis that higher comorbidity will increase patient delay.

#### **Psychosocial Factors**

Social, cognitive, and emotional factors may contribute to patient delay. Many studies have explored the psychosocial determinants of delay<sup>38,42,124,125</sup>. Not surprisingly, three studies found a positive association between utilizing a denial

type of defence mechanism and patient delay. In contrast, Watson<sup>125</sup> found no such association.

The results of Antonovsky's review<sup>105</sup> suggested that fear, anxiety and emotional responses in relation to the discovery of a breast cancer symptom influenced the timing of help-seeking. Where two studies supported anxiety as a significant predictor of the intention to delay care seeking<sup>126,127</sup>, three other studies found no relationship between anxiety and patient delay<sup>39,125,128</sup>. The inconsistent results may be explained by several methodological concerns, including descriptive study designs, and potential bias from uncontrolled confounding. Furthermore small sample sizes and sample selection criteria raise serious concerns about the generalizability of these studies.

2.4.2 Provider delay (System delay)

Determinants of provider delay in diagnosis and treatment of breast cancer have been studied much less extensively. In a recent review of literature, Ramirez et al.<sup>104</sup> reported on the most relevant studies since 1960. Although twenty-eight papers were identified as containing original data of potential risk factors for provider delay, only eight met the pre-defined quality selection criteria for inclusion in their review. The determinants of provider delay can be grouped into three major components: patient profiles, provider characteristics, and hospital factors.

#### Patient profiles

1) Age

Most research has demonstrated that patient age is a strong predictor of physician delay. The age effect is opposite to the effect observed on patient delay. Older women are less likely to be subjected to longer provider delay, especially white older women<sup>129</sup>. The Physician Insurance Association of America (PIAA) study reported that important factor increasing physician delay to diagnosis of breast cancer was observed for younger women presenting with self-discovered breast lump<sup>130</sup>. A Singapore study also supported increased provider delay in relation to younger age. Women under 35 years of age experienced increased physician delay (65%) compared to women over 35 years (8%)<sup>108</sup>. Although 15 studies identified by Ramirez et al<sup>104</sup> found age to be associated with provider delay, only 5 studies met their inclusion criteria. Of those five, four studies supported the hypothesis that younger age is a risk factor for provider delay<sup>15,48,129,131</sup>.

The effect of age might be explained by the fact that younger women have a much lower incidence of breast cancer. In young women, especially those in their thirties, there is a high incidence of benign breast diseases. Therefore, physicians might be less suspicious of breast cancer and may less aggressively evaluate breast symptoms, increasing provider delay. Another reason might be greater likelihood of mammographic density in young women, increasing the risk of a false negative mammogram leading to delay to treatment.

This association however, has not been consistent across studies. Bywaters<sup>46</sup> didn't detect this association; however this may be a result of small sample size. Age may affect how physicians make decisions about patterns of care for breast cancer patients. After controlling for comorbid conditions, functional status, tumour

stage, and type of hospital, Greenfield et al.<sup>132</sup> found that physicians provided less optimal care for older patients.

2) Race

The reports about the relationship between race and provider delay have been inconsistent. Dennis<sup>80</sup> found that among 237 breast cancer patients at a city hospital in United States in 1960s, there was greater physician delay in treatment for black women than for white women, especially in the younger age groups. A recent study demonstrated similar results<sup>129</sup>. McWhorter et al.<sup>133,134</sup> showed that blacks receive lower quality care compared to whites, both in terms of receiving appropriate treatment for breast cancer, and the likelihood of receiving more aggressive therapy. The authors suggested that access to health care might be a reason producing this difference. An investigation has indicated that in general, black Americans do not use the medical care system to the same extent or in the same way as white Americans<sup>135</sup>.

Race might affect provider delay by acting as a proxy for income and education, with black women tending to be poorer and less educated and, therefore, having decreased access to medical care in United States. However, in their review, Ramirez et al.<sup>104</sup> also reported that there was evidence that non-white women have longer provider delay.

3) SES and Education

Ramirez et al.<sup>104</sup> also found that there was insufficient evidence to conclude about the effect of socioeconomic status since only one study contributed to review for this factor. Benk et al.<sup>55</sup> concluded that lower income breast cancer women did not wait longer for radiation treatment than higher income patients. This was possibly a result of the Canadian universal healthcare system that provides the same health care to everyone. Patient educational level has not been reported in any study as a factor influencing the physician delay.

#### 4) Presentation of Symptom

Non-lump presentation (pain, skin changes and nipple discharge, etc.) has been the most common reason for delay in diagnosis of breast cancer as the lack of physical findings have failed to impress the physician as to the possibility of breast cancer<sup>45,48,129,130</sup>.

#### 5) Health Status and Comorbidity

The results from community-based studies have demonstrated that women in good health are less likely to get a screening mammogram than those with chronic conditions<sup>136-138</sup>. The fact that healthier women are less likely to have regular contact with a physician may contribute to this association. Another factor that has been associated with delay within health services is the history of benign breast disease<sup>45</sup>. However, there is no study that has explored how comorbidity or the history of benign breast disease influence diagnostic and treatment delay.

#### **Provider Characteristics**

#### 1) Gender

There are very few studies that have examined the effect of physician characteristics on provider delay. One study suggested that the gender of the physician might influence delay. Thirty-three percent of women were embarrassed to have a male doctor examine their breasts and 50% preferred a female doctor<sup>47</sup>.

#### 2) Misdiagnosis of breast diseases

Misdiagnosis of benign breast disease, mastitis or symptoms without breast diseases, such as weaning and stress were common reasons for delay after women were in the health care system<sup>139</sup>. In their sample of 165 breast cancer patients, Mann and co-workers<sup>140</sup> found that 36 (34%) women experienced false normal mammograms. Of which, 53% had biopsies delayed for three to 24 months. Others reported that a false negative mammogram is common in women younger than 50, and may lead to treatment delay and advanced clinical stages at diagnosis<sup>141,142</sup>.

#### 3) Age and year of graduation

Early studies examining the effect of physician experience upon the quality of care have reported that younger physicians generally perform better than older physicians<sup>143-145</sup>. The period in which a physician receives basic training or the length of time since graduation influences the adoption of new procedures. Older physicians have been found to be less likely to practice innovations for the earlier

medical training has an enduring influence on practice<sup>146,147</sup>. In contrast, others have found no quality of care difference with the years of physician practice<sup>148</sup>.

4) Patient volume and physician density

There is evidence that in geographic areas where physician density is relatively high, practice styles are more aggressive than in less competitive communities<sup>149</sup>. The greater the physician density, the greater the likelihood that appropriate care was provided<sup>150</sup>. An adequate patient volume has been linked to acceptable performance of hospital units and individual physicians<sup>147,151</sup>.

The effects of physician age, year of graduation, practice volume and practice preference on the provider delay have not been previously explored. We assume these factors may influence the pattern of breast cancer care, thus influencing provider delay. For older physicians, or those who graduated years ago, we might expect a less complicated pattern of investigations and thus a shorter time interval between procedures. The delay would be expected to be shorter for physicians with larger breast cancer patient volumes related to their experience in treatment and decision making.

#### Hospital Factors

There were few studies examining hospital factors that could influence delay for the diagnosis and treatment of breast cancer. In their study of 162 breast cancer patients, Adam et al.<sup>45</sup> found that there were administrative delays, including obtaining an outpatient appointment and a hospital bed. However, their study was

descriptive without statistical tests and the finding could have been due to chance. Several recent studies found that the elapsed time to treatment was significantly longer for women seen in public hospitals than in private practice<sup>53,139,152</sup>. Wall<sup>153</sup> suggested that in an urban public hospital, provider delay may be related to inadequate access to surgical consultation and operating rooms. He implied that the lack of surgical manpower and surgical room resources are part of the reasons for delay. From an analysis of cancer registry data in Chicago, Hand et al.<sup>154</sup> suggested that late stage at diagnosis was associated with hospital urban location, fewer breast cancer cases treated, and lower oncology charges.

By comparing health care for cancers in many sites in US and in Canada, Mackillop<sup>51</sup> concluded that treatment delay may be due to differences in the organisation of cancer services in the two health care systems. "(1) Canadian cancer centres are usually the sole providers. (2) Patients are an economic liability to a Canadian center operating on a global budget and there would be no immediate financial impact on the institution if referrals did decline. (3) Doctors and institutions in Canada are under much less threat of litigation than they are in USA".

1) Volume and Size

Hospital size, medical school affiliation, volume and organisation of cancer services in the health care system are factors that have been found to related to waiting times for radiotherapy after surgery received by breast cancer patients<sup>51,132</sup>. There is evidence that hospital geographical location and hospital

teaching status are associated with an increased likelihood of having breastconserving surgery<sup>155</sup>. Hospital size was found to have a significant and consistent negative effect on whether appropriate care was provided.

Furthermore, a study of delay between surgery and radiotherapy in Montreal demonstrated that delays were significantly less for women referred from a community hospital than from a university hospital<sup>55</sup>. This may reflect a high patient volume in teaching hospitals and more complicated procedures of care. Kelly<sup>156</sup> found an inverse relationship between surgical patient mortality and the total volume of specific surgical procedures performed in the hospital.

2) Other hospital factors

Mistaken diagnoses, administrative errors, or unduly long waiting lists for admission have been discussed as the usual sources of the delay for general diseases<sup>2</sup>. Although a further study reported that staff caseloads had no effects on waiting time of treatment for carcinoma of the larynx, the equipment workload was an important factor affecting the waiting time<sup>51</sup>. However, no study has reported the determinants of provider delays for breast cancer surgery.

In sum, although hospital factors may play an important role in provider delay, there is no study on the variation of waiting time for the diagnosis and surgical treatment among hospitals. We assume that the pattern of care and the decisions made for management of breast cancer would be strong factors in the variation of waiting time. This was the case at both the hospital and geographic level in the

use of breast conserving surgery procedures for the management of breast cancer<sup>157,158</sup>.

A summary of the literature related to the system delay of breast cancer treatment is given in table 2.5. In conclusion, provider delay has been largely underresearched with only few descriptive studies performed within single institutions and with small sample sizes. Although considerable research on hospital and geographic variation in the type of surgery for breast cancer has been undertaken in both Canada and the United States, waiting time has not been examined<sup>157-159</sup>.

#### 2.5 Methodological Issues in the Study of Delay

The term 'delay' refers to a longer than expected waiting time, and has been used in previous studies. However, there are several concerns about using this terminology. First, the term delay has a negative connotation, implying that any time elapsed between the breast cancer procedures is longer than expected and would lead to poorer outcome. This is not always the case, as both the women and their physicians need reasonable time to make decisions regarding the appropriate course of treatment. In addition, a period of waiting time may be required due to the biological nature of the disease. For example, survival time after surgery for breast cancer might be influenced by the timing of the surgery, which in turn is related to the immunological defence mechanism, which varies during women's menstrual cycle<sup>160-162</sup>. In these instances, it is not reasonable to define delay as counting the entire time interval between two procedures. Second, the choice of a criterion for distinguishing delay from no-delay is arbitrary. The literature shows that there are many different criteria and definitions of delay, which makes it difficult to compare between studies. It is still unknown what the standard for reasonable waiting time is. Finally, to dichotomize the waiting time as delay or not delay results in a loss of information.

The majority of investigators defined patient delay as the total time elapsed from the initial discovery of a breast disease symptom until the first visit to a healthcare professional. Sometimes this period may include a component of provider delay, such as waiting for a doctor's appointment. Furthermore, patients themselves may contribute to some proportion of the delays that occur after entering the health care system, such as patients missing or postponing their appointments. Therefore, estimating the proportion of the variation of waiting time that is attributed to the health care system and the patients is important in order to provide specific information needed to identify population level strategies at hospital, physician, and patient levels to reduce delays.

Most studies of patient delay included their subjects after diagnoses with breast cancer and information was retrospectively collected by interview or self-administrated questionnaire. This approach introduces the potential for recall bias. Women who knew that they had a serious illness or advanced breast cancer were more likely to report a period of delay and to recall the potential risk factors of delay <sup>104,105</sup>,.

The studies completed to date have generally been of poor quality in terms of both their theoretical basis and the methodology used. Many of these studies used a

simple descriptive only approach reporting the proportion of the delay, without the use of more informative statistical analytical procedures. Other limitations in these studies included the use of small sample sizes and/or unrepresentative samples, where patients were selected based on non-systematic recall by physicians of women who had extreme periods of delay.

#### 2.6 Summary and Justification of the Research

The review of the literature related to the diagnosis and treatment of breast cancer portrays the complicated pattern of care that a woman with a potential breast cancer must endure. Therefore, studying the pattern of care for breast cancer will provide fundamental information needed to simplify the diagnostic process, hopefully making it less stressful. Little research has been done on system delay, especially in Canada where the universal health care system is quite different from that of many other countries. Through the guidance of a conceptual framework that reflects the relationship between the predictors of long waiting time for breast cancer diagnosis and treatment procedures, this study will assess three levels of determinants, which are patient profiles, physician characteristics, and hospital factors.

There is general agreement that previous studies on delay for breast cancer care are generally of poor quality, and there is a need for further primary research. The methodologies of these studies were problematic in terms of the design and statistical analysis used. Unaccepted delay time by patients and providers are clearly multifactorial and complex. Multivariate analysis is certainly needed to

improve our understanding of the factors that increase the risk of delay. This study will estimate a three level hierarchical data structure, which includes women with breast cancer nested within physicians, and physicians within the hospitals. Patients who come from the same physician or the same hospital may have similar factors influencing their waiting time. As a result, the average correlation expressed as an intra-class correlation between variables for patients from the same hospital or who have the same physician will be higher than for patients who are from different hospitals or physicians. Ignoring such clustering effects will violate the assumption of independent responses required by traditional regression methods. As a result, the standard error of the effect of a variable on the outcome of waiting time is underestimated, leading to an increase of the probability of a type | error<sup>163</sup>. The simultaneous assessment of patient, physician, and hospital level variables calls for a statistical approach that accounts for the hierarchical structure of the data. To date, this approach has never been used in this area of research.

One of the objectives of this study is to assess hospital variation of waiting time for breast cancer procedures and provide information that will be useful for improving services. From the literature it is clear that there is geographical and institutional variation in the preferred pattern of care for breast cancer. We expect to see significant variation in waiting time between hospitals, and we expect that the variables that will explain this variation include pattern of care, patient volume, hospital structure, geography location of hospital, and services provided by the institute.

The determinants of waiting time in the health care system for breast cancer surgery have not been systematically studied. The incidence of breast cancer continues to rise and the delayed detection and treatment of breast cancer has been associated with negative clinical and psychological factors such as distress, fear, anxiety, and depression. Since it is not known whether this is also an effect on outcome, it is crucial that efforts be made to reduce any kind of unnecessary waiting time. A first step towards achieving this goal is to conduct a study to discover the determinants of longer waiting time at the level of the woman, physician, and hospital that in turn would provide valuable information for intervention on the targeted objectives. This question can be comprehensively studied owing to the development and maintenance of universal computerized databases of physician services. To understand where longer waiting comes from and why there is variation among different centres, the waiting time for treatment of breast cancer as women go through the healthcare system needs to be examined. This is necessary for developing strategies directed towards minimizing waiting to diagnosis and treatment in the province of Quebec and across Canada. Reducing periods of delay is something that is potentially preventable and manageable and can have a positive impact on the psychological well being, quality of life, and potentially even the survival of women with breast cancer.



\*SBE: self breast examination

# Figure 2.1 Pathway of Breast Cancer Diagnosis



Figure 2.2 Pathway of Breast Cancer Treatment

First Author	Country	Year published	Definition of delay	Data source	Sample (N)	% of women delayed	Median Time (days)
Caplan	U.S.A.	1996	> 2 months	Administrative database	367	25	
Caplan	U.S.A.	1995	> 2 months	Interview	162	16	
Coates	U.S.A.	1992	>2 months	Questionnaire	735	26	16 days
Katz	U.S.A. and Canada (BC)	1993	> 3 months	Tumour registry	174 195	17 16	11 days 8 days
Mor	U.S.A.	1990	≥3 months	Interview	298	32	
Freeman	U.S.A.	1989	≥3 months	Chart review	193	56	
Samet	U.S.A.	1988	≥3 months	Interview	189	25	
Vernon	U.S.A.	1985	≥3 months	Questionnaire	3061	44	
Gould-Martin	U.S.A.	1982	> 3 months	Interview	274	21	
Huguley	U.S.A.	1981	≥3 months	Questionnaire	2092	21	
Wilkinson	U.S.A.	1979	≥3 months	Administrative data base	1784	32	
Safer	U.S.A.	1979	-	interview	93	_	Median=8 Mean=57
Dennis	U.S.A.	1975	≥3 months	Chart review	237	48	

	Table 2.1 Patient Dela	v: Summarv	of literature on	time from bre	ast symptoms to	professional consultation
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Table 2.1,	Patient I	Delay:	continued.
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First Author	Country	Year published	<b>Definition of</b> delay	Data source	Sample (N)	% of women delayed	Median Time (days)
Hackett	U.S.A.	1973	>3 months	Questionnaire	563	39	
Richards	Great Britain	1999	> 3 months	Cancer registry	2964	20-30	
Burgess	Great Britain	1998	≥3 months	Interview	185	19	
Nichol	Great Britain	1981	≥3 months	Interview	72	40	16 days
MacArthur	Great Britain	1981	≥3 months	interview	145	31	
Adam	Great Britain	1980	≥3 months	Interview	168	24	
Rossi	Italy	1990	≥3 months	Interview	189	36	60 days
GIVIO	Italy	1986	≥3 months	Chart review	1110	36	
Robinson	Israel	1986	>6 weeks	Chart review	523	43	
Antonovsky	Israel	1974	> 3 months	Literature review	-	35-50	
Afzelius	Denmark	1994	>2 months		7,608	24	
Menon	Singapore	1992	≥3 months	Chart review	359	40	
Wang	China, Taiwan	1993		Interview and questionnaire	71		1 -24 weeks
Williams	Wales	1978	> 3 months	Interview	158	23	
Total			> 3 months	27 studies	23,969	29	

First Author	Place	Year published	Data source	Sample	Definition of delay	% of delay over three months	Median waiting time (range)
Мауо	Canada (Quebec)	2001	Administrative database	29,606	Initial diagnostic procedure to first surgery, ≥3 months	14	34
DeCoster	Canada (Manitoba)	1999	Administrative data		Last surgical visit to surgery		16
Benk	Canada (Montreal)	1998	Chart review	739	Surgery to radiotherapy No chemo (NC)>7 weeks With Chemo(C)>24 weeks	54 delayed overall; 72 in group•NC; 21 in group C	
Mackillop	Canada (Ontario)	1994	Administrative database	4971	Diagnosis to initiation of radiotherapy		61.4
Tartter	U.S.A.	1999	Chart review	1014	First consultation to final diagnosis, > 3 months	8	
Wall	U.S.A.	1998	Chart review	146	First consultation to final diagnosis		78.6
Caplan	U.S.A.	1996	Administrative database	367	Initial consultation to final diagnosis, > 2 months	45	
Caplan	U.S.A.	1995	Administrative database	996	Initial consultation to final diagnosis, > 3 months	17	15-18
Katz	U.S.A. Canada	1993	Tumour registry	174 195	Final diagnosis to initial surgery	3 2	10 6

Table 2.2 System delay: Summary of literature related to system delay for breast cancer from the presentation to the health care system to diagnosis, or treatment

First Author	Place	Year published	Data source	Sample	Definition of delay	% of delay over three months	Median waiting time (range)
Katz	U.S.A. Canada	1993	Tumour registry	174 195	First contact to final diagnosis	13 5	17 days 16 days
Mann	U.S.A	1983	Chart review	36	False normal Mammogram to biopsy, > 3 months	53	
Richards	Great Britain	1999	Administrative database	2964	First visit to referral to hospital, Greater than 3 months	6-16	
Nichols	Great Britain	1981	Interview	72	Referral by a doctor to hospital outpatient clinic		9 days
Adam	Great Britain	1980	Chart review	168	Attending hospital to receiving treatment	23	
Joensuu	Finland	1994	Interview	306	False negative mammogram to surgery, > 6 months	29	
Menon	Singapore	1992	Chart review	359	First consultation to biopsy, > 3 months	28 (women< 35 years old)	
Rossi	Italy	1990	Interview	189	From medical diagnosis to treatment		15 (4-47) days
GIVID	Italy	1986	Chart review	1110	First visit to final diagnosis	14	
Robinson	Israel	1984	Chart review	412	First visit to final diagnosis, >6 weeks	42	
Williams	Wales	1978	Interview	158	First visit to referred to a hospital	10	

Table 2.2 System delay, continued

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Hypothesized Outcome	Total	Support	No effect
Increased tumour size	5	5 <sup>74-76,78,79</sup>	0
Higher stage of disease	12	<b>11</b> <sup>7,11,83,84,90,96,100,164-167</sup>	1 <sup>9</sup>
Recurrence of cancer	3	<b>1</b> <sup>55</sup>	<b>2</b> <sup>9,80</sup>
Decreasing survival	30	<b>22</b> <sup>5,11,14,36,41,83-95,100,101,166,167</sup>	<b>8</b> <sup>7,9,80,96-99,168</sup>
Increasing stress	6	<b>6</b> <sup>67-72</sup>	0
Decreasing quality of life	2	<b>2</b> <sup>81,82</sup>	0

# Table 2.3 The number of studies investigating the hypothesized impact of patient and provider delay on breast cancer outcomes

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Hypothesis (Risk factors for patient delay)	Number identified	Studies supporting hypothesis	Studies not supportin hypothesis
Sociodemographic factors	 		
Older age	27	15 studies <sup>15,43,44,46,47,102-106,</sup> 112,169-172	12 studies <sup>8,10-12, 41,45,</sup> 48,80,108,109,113,123
Non-white ethnic origin	13	<b>11</b> studies <sup>44,80,84,112,114,115,118, 170,172-174</sup>	2 studies <sup>106,126</sup>
Lower socio- economic status	15	10 studies <sup>12,38,83,105,106,111,112,</sup> 115, 122,170	5 studies <sup>44,48,106,113,12</sup>
Lower educational level	7	4 studies <sup>47,105,111,112</sup>	3 studies <sup>8,106,113</sup>
Unmarried	6	0	6 studies <sup>8,10,101,104,</sup> 110,123
Clinical factors			· · · · · · · · · · · · · · · · · · ·
Discovery of breast symptom other than a lump	13	10 studies <sup>12,40,45,48,85,102,104,</sup> 115,122,175	3 studies <sup>10,113,123</sup>
History of benign breast diseases	2	2 studies <sup>12,45</sup>	
comorbidity	2	2 studies <sup>43,122</sup>	
Psychosocial factors		······································	
Anxiety	5	2 studies <sup>126,127</sup>	3 studies <sup>39,125,128</sup>
Fear	4	4 studies <sup>105,109,113,176</sup>	
Denial	3	2 studies <sup>123,124</sup>	1 study <sup>125</sup>

## **Table 2.4 Predictors for Patient Delay**

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Hypothesis (Risk factors for provider delay)	Number identified	Studies supporting hypothesis	Studies not supporting hypothesis
Patient profile			
Younger age	10	8 studies <sup>15,48,104,108,129,</sup> 131,140,142	2 studies <sup>45,46</sup>
Non-white ethnic origin	4	1 study <sup>118</sup>	3 studies <sup>80,129,177</sup>
Lower socio-economic status	2		2 studies <sup>55,129</sup>
Physician characteristics			<u></u>
Male physician	1	1 study <sup>47</sup>	
Misdiagnosis or false negative mammogram	8	8 studies <sup>40,45,52,110,139-</sup> 141,178	
presenting of breast symptom other than a lump	5	5 studies <sup>45,104,129,175,179</sup>	
Hospital factors			
Public hospital	4	4 studies <sup>53,129,139,170</sup>	
Administrative factors	3	3 studies <sup>45,110,180</sup>	

### Table 2.5 Predictors for Provider Delay

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Table 2.6 Pattern of Care, Summary of Literature Review									
Author	Setting	Year of publish	Data resource	Outcome	Factors studied	Conclusion			
Hebert-Croteau <sup>181</sup>	Quebec	1999	Quebec Tumour registry, MedEcho	Proportion of BCS and use of other systemic adjuvant therapy	Hospital caseload, involvement in clinical research	Large centres, involved in clinical research provided better care			
Hebert-Croteau <sup>182</sup>	Quebec	1999	Quebec Tumour registry, MedEcho, Medical charts	Proportion of BCS and use of other systemic adjuvant therapy	Patient age, Hospital caseload, comorbidity, year of dx, graduation year of MD, estrogen receptors, tumour grade	Less aggressive patterns of care are provided to elderly patients.			
Iscoe <sup>157</sup>	Ontario	1994	Ontario cancer registry, death registration,	Proportion of BCS	Location of surgery, hospital volume, county caseload, teaching status, radiotherapy, age of patient,	Large variation at hospital & county level in use of BCS.			
McGinnis <sup>230</sup>	United States	2000	The National Cancer Data Base	Describe age, stage, histology grade, type of treatment	Zip code income level, geographic area	Improvement in the early Dx and surgical Tx of low income patients can be achieved			

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Author	Setting	Year of publish	Data resource and sample size	Outcome	Factors studied	Conclusion
Farrow <sup>159</sup>	United States (9 area)	1992	Surveillance, Epidemiology, & End Results Program;	Proportion of BCS & radiotherapy after BCS	Age, race,	Large unexplained variation in use BCS
Nattinger <sup>158</sup>	United States	1992	Medicare claims, Hospital discharge	Proportion of BCS	Size of area, teaching status, number of beds, full-time house staff, owner of hospital; race, severity,	Large unexplained geographic variation in BCS. Teaching status, availability of service are strong predictors for BCS

#### Table 2.6 Continued. Pattern of Care, Summary of Literature Review

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# Chapter 3. Article 1

#### **Preface to Article 1**

Results of the main project, waiting time for breast cancer surgery in Quebec<sup>183</sup>. showed that (1) waiting time had increased significantly over time between 1992 and 1998, and (2) the process of care, especially the number of procedures women received before their surgery was found to be an important contributor. Therefore, the first article in this thesis describes the pattern of care received by women with surgically treated breast cancer and identifies determinants of the pattern of care. These two steps are necessary in order to examine determinants of waiting time, which will be the focus of the second article. Other studies have considered the pattern of care for breast cancer from the view of variation in the type of surgery performed <sup>157,181,184</sup>. In our study, waiting time was defined as the time interval from the beginning of the first diagnostic procedure to the definitive surgery, covering the major process of care for the breast cancer episode. We felt that the type of diagnostic procedures and the number of procedures received before surgery would also be important components of the pattern of care. To understand the pattern of care for women with breast cancer and the factors determining variation in patterns of care would help us investigating the determinants of waiting time.

In the first article, we describe patterns of care, including type of procedures performed and the number of procedures received before surgery, using existing

information in the database. Furthermore, we identify factors influencing variation in the number of procedures received before surgery and in the use of breast conservative surgery.

## Article 1: Factors Associated with Patterns of Care for Breast Cancer

## in Quebec between 1992 and 1997

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#### INTRODUCTION

The availability of programs for early detection of breast cancer combined with effective interventions has had a favourable impact on survival and quality of life<sup>96,185</sup>. All steps in the process of care (detection, diagnostic work-up, and treatment) are important to the outcome of breast cancer. The two guiding principles of the Canadian Practice Guidelines for breast cancer are to establish an accurate diagnosis with a minimum number of procedures and to select the optimal treatment regimen for each woman<sup>1</sup>. The use of additional diagnostic procedures may potentially delay treatment and, thus, may lead to sub-optimal clinical and psychological outcomes<sup>69,186</sup>.

With a condition as complex as breast cancer, affecting women over a wide range of ages, some variation in pattern of care is expected because of reasonable differences in physicians' judgements or women's preferences. Other differences in patterns of care may be outside the accepted norms of good practice. Irrespective of the reason, variation in providing appropriate care can be a source of anxiety to patients.

Most of the literature describing variations in pattern of care for breast cancer has focused on treatment<sup>157,181,187</sup> or on the diagnostic accuracy of procedures<sup>188,189</sup>. Iscoe et al. found large variations in the use of breast conserving surgery (BCS) across Ontario hospitals and counties during 1989 to 1991; the proportion of women receiving BCS ranged from 6% to 84%<sup>157</sup>. In 1991, the average use of

BCS in Ontario was higher than that reported from British Columbia for the same year (68% vs 44%)<sup>184</sup>. In Quebec<sup>181</sup>, for the period 1988 to 1994, BCS use for early stage primary breast cancer varied from 76% to 88%, with the highest rates found in hospitals having the highest volumes.

The factors most commonly studied for their relationship to variation in type of surgery are hospital factors such as access, volume, and teaching status<sup>154,155,190</sup>. Patient-related factors have been included mainly for purposes of adjustment and have not often been the primary focus<sup>159,181,184</sup>. Lower use of BCS does not necessarily imply sub-optimal care, for example, women who live in remote areas may not wish to travel long distances to receive the type of follow-up therapy required after BCS<sup>191</sup>.

Understanding variations in diagnostic work-up before surgery for breast cancer would help to assess the quality of care provided to Canadian women. In a recent study in Quebec (1992 –1998)<sup>183</sup>, we found that the median time from the initial procedure to definitive surgery was 34 days (interquartile range 18 to 58 days), and 13% of women waited for more than 90 days. The median time to surgery more than doubled for each two additional diagnostic procedures. The specific objective of this study is to estimate variation in three aspects of the pattern of care for breast cancer, type of surgery, type of diagnostic procedures, and number of procedures, and to identify factors contributing to the variation in pattern of care.

#### METHODS

#### Data Source and Study Population

The data for this study were extracted from the database of physician fee-forservice claims maintained by the Régie de l'assurance maladie du Québec (RAMQ), the Quebec hospital discharge database (MedEcho), and the 1991 Canadian census.

The RAMQ services database was used to identify all records of women age 20 years and older who between 1992 and 1997 had at least one billing for an invasive diagnostic or curative procedure related to the breast. We obtained data from 1989 to identify previous breast disease or breast-related procedures.

To identify which women were surgically treated for breast cancer, we identified those RAMQ billings that matched a record of a hospitalization or day-surgery on the Med-Echo database. The two databases used different systems for coding procedures (the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP) for MedEcho and an internal system for RAMQ [http://www.ramq. gouvqc.ca/pro/pro.html]), and these data were consolidated and reconciled. Although over 90% of the records agreed on surgical procedure and date, leeway was permitted to include records where there were minor discrepancies in date and type of procedures. Surgery was considered to be for breast cancer when there was a record of a hospitalization or day-surgery (Med-

Echo database) including a diagnostic code for breast cancer. The treatment date for newly diagnosed breast cancer was defined as the date of the first surgery.

Breast cancer was classified according to the Ninth Version International Classification of Diseases (ICD-9 174.0-174.9, 233.0, 238.3). Also included were women with a diagnostic code for secondary lymph node involvement (196.0-196.9) or metastatic disease (197.0-199.0), provided a prior diagnosis of breast cancer had been made.

Procedures were grouped into "episodes" by combining consecutive procedures that were within five months of each other and that included surgery for breast cancer. The five-month period was chosen to avoid combining procedures for routine follow-up commonly recommended at six-month intervals<sup>192</sup>. No restriction was placed on the total cumulative duration of an episode. Only 3.7% women had more than one episode; in these instances, only the first episode was retained in the analysis.

#### Measurements

The specific care practices that were evaluated for variation across women, surgeons and hospitals were the use of BCS and the number of diagnostic procedures performed before surgery. Women's characteristics included age, cancer stage, co-morbidity, history of benign breast disease and socioeconomic status.

To ensure confidentiality the age of subjects (in 1992) was available only in fiveyear groups. Using the MedEcho ICD-9 diagnostic codes, stage of breast cancer was classified as: "localized" if only a diagnosis of primary breast cancer was recorded; "regional" if a code for secondary cancer of the axillary lymph nodes was also present; and "disseminated" if metastases beyond lymph nodes were recorded; and "uncertain" if breast neoplasm of uncertain behaviour was coded. In addition, we defined a category for carcinoma *in situ*.

The Charlson Comorbidity Index was calculated for each woman using the method described by Romano et al.<sup>193</sup>. This index identifies co-morbidity from the 15 secondary ICD-9 diagnoses available on the MedEcho database; the one-year time period before diagnosis was chosen to calculate co-morbidity. In addition to this index, history of benign breast disease in the 3 years before the index episode of care was defined using diagnostic codes (ICD-9: 217.0-217.9, 610.0-610.9) in the MedEcho database and/or procedure codes for the treatment of benign breast disease listed in the RAMQ database (0444, 0594, 1011, and 0821).

We had no direct information on socioeconomic status. Instead, we created surrogate variables by linking each woman's 6-character postal code to the 1991 Canadian Census. The median household income and the proportion of the population who did not complete high school in each woman's postal code area of residence were calculated. The distance from each woman's place of residence to

the nearest tertiary medical center, mammography center, and acute-care hospital was also calculated and used as a proxy for access to care<sup>194</sup>.

Only one surgeon was assigned to each woman and this individual was identified using RAMQ codes for primary surgeon. The following characteristics of this primary surgeon were used in the analysis: the average annual numbers of breast surgeries performed; school of graduation; and age in 1992. To maintain confidentiality, the gender of the surgeon was not made available to us.

The hospital in which the surgery was performed was identified from the MedEcho database through a unique, encrypted, hospital code. Teaching status was assigned to each hospital using information provided by the RAMQ. Using the available data, four other variables were created for each hospital. The average annual number of hospital discharges for breast-related diseases, including but not limited to breast cancer was calculated (this was done to reflect breast disease expertise). We also calculated the proportion of women attending the hospital for breast-related disease who lived more than 100 km away, who lived in a "low-income" area, and who lived in an area with a high proportion of individuals who did not complete high school. Although a finer categorization for these variables was originally proposed, analyses revealed the appropriateness of these cut-points.

#### **Statistical Analysis**

The analyses focused on identifying factors associated with: (1) the expected proportion of women having BCS versus mastectomy; and (2) the expected proportion of women receiving three or more diagnostic procedures. The data structure is hierarchical with three levels: women are clustered within physician's practice and physicians are clustered within hospital. The main statistical issue is that the pattern of care for women treated in one hospital will likely be more similar, on average, than the pattern of care for women from different hospitals. Thus, analyses using traditional regression methods including variables at all three levels but ignoring the effect of clustering would underestimate the standard error and inflate the type I error<sup>163</sup>. The bias would arise because the residuals for observations in the same cluster are correlated, violating the independence assumption.

To account for the cluster effects, hierarchical logistic regression models, estimated using penalized maximum quasi-likelihood (PQL)<sup>195</sup>, were implemented with MLwiN software<sup>196</sup>. To illustrate the method, the first step in the analysis involved partitioning the total variability of the proportion of BCS into within-surgeon, between-surgeon, and between-hospital components by fitting a random intercept model. Step 2 involved identifying attributes of women (level-1) with significant fixed and/or random effects on the proportion of BCS. This was done by first fitting a series of univariate models, one for each of the level 1 predictors listed in Table 1. Attributes retained for inclusion in the multivariable level 1 model were those for which either fixed or random effects were significant at the 0.10

level. A significant fixed effect implies that the average effect of women's characteristics on the BCS use is different from the null, and a significant random effect implies variation across surgeons and hospitals. The third step involved including the effects of surgeon- (level 2) and hospital- (level 3) factors on the BCS use; the significance level for inclusion was set at 0.10. To assess what proportion of the unexplained variance across hospitals in the use of BCS can be explained by hospital-specific characteristics, we compared the variances obtained from the model with woman and surgeon characteristics only to the model in which hospital characteristics were added. The regression coefficients for each fixed effect variable were used to calculate odds ratios (OR) and 95% confidence intervals (95% CI). Potential interactions between selected woman's characteristics were evaluated one at a time at the 0.05 significance level while adjusting for all other variables in the model.

The estimated co-efficient from the multiple logistic regression model was used to calculate the predicted probability of a woman with a given risk profile receiving a BCS. Then, the adjusted relative risk was calculated as the result of probability for different values of a given variable.

#### RESULTS

A total of 24,591 women with diagnosed breast cancer in the index period were identified. Excluded were women with a diagnosis of breast cancer before the index study period (n=175), without surgical treatment (n=411), or who underwent

chemotherapy before surgery (n=635). Surgeries were performed by 724 surgeons in 109 hospitals. Table 3.1 shows the characteristics of the women, the surgeons, and the hospitals. One-third of the women were less than 50 years of age and 11% were 75 years of age and older. Two-thirds of women had localized breast cancer, while one quarter had breast cancer with lymph node positive. Eighty percent of surgeons performed fewer than 10 breast cancer operations a year. One half of hospitals providing treatment for breast cancer were classified as affiliated to a university and 55% of hospitals had fewer than 100 women per year hospitalized with breast disease.

Table 3.2 shows the types and numbers of procedures carried out over the sixyear study period. Overall, 80% of women received BCS and 83% of women had at least one bilateral mammogram. Twenty-three percent of women had three or more procedures before their surgery, and 5.6% had no recorded procedures before surgery. Figure 3.1 describes the distribution of the first two procedures and the proportions whose third procedure was surgery. The type of the second procedure varied depending on the first procedure performed (chi-square test, p<0.0001). Most women (78%) had a bilateral mammogram as their first procedure and 11% started with a biopsy. Of the women who began with a bilateral mammogram, one-third went to surgery and 40% had a biopsy. For women who started with a biopsy, 42% went to surgery but 46% received a bilateral or unilateral mammogram, and about 11% received another biopsy.

There were statistically significant differences in the use of certain diagnostic procedures according to the distance to a health center. Women living more than 100 km away from their treating hospital were less likely than women living nearby to undergo a core biopsy (5.4% vs. 10.1%, p<0.0001) and unilateral mammogram (6.8% vs. 10.3%, p<0.001), but were more likely to have an ultrasound (34.1% vs. 13.8%, p<0.0001).

## Variations in Use of BCS

The estimated fixed effects of individual-, surgeon- and hospital-related factors on the use of BCS are presented in Table 3.3. Presented in this table are the crude proportions of BCS use for different levels of co-variates. Adjusted proportions were quite close to the crude proportions and for simplicity we present only the crude values. Odds ratios, adjusted for all other variables listed in the table, are also presented. Odds ratios less than unity mean that there was a lower proportion of women with that particular level of covariate receiving BCS. The proportion of women who underwent BCS was significantly lower among women who were: older than 70 years of age (65% vs. 85%), with advanced stage of tumour (68% vs. 94%), with comorbidity (68% vs. 81%), with history of benign disease (76% vs. 80%), living in an area with lower household income (76% vs. 86%), and living more than 100 km from the treating hospital (76% vs. 81%). After adjusting for women's characteristics, there were no significant relationships between the surgeons' characteristics and the proportion of their patients who

received BCS. Hospitals with fewer annual numbers of breast disease discharges were less likely to use BCS compared with hospitals with larger number of these discharges (72% vs. 86%).

#### Variation in Numbers of Procedures

Table 3.4 shows associations with the probability of receiving three or more procedures before surgery. Presented in this table is the distribution of women according to number of procedures prior to surgery. Also presented are adjusted odds ratios comparing women with three or more procedures to women with one or two procedures. The proportion of women who received three or more procedures increased from 19% to 29% over the six years of study (test for trend, p<0.001). The adjusted probability of receiving three or more diagnostic procedures prior to surgery was significantly higher during the two most recent years (ORs of 1.19 and 1.41 for 1996 and 1997, respectively) as compared with 1992. Women with lymph node involvement or disseminated cancer had fewer procedures than did women with localized cancer. None of the socioeconomic characteristics were associated with the number of procedures received and, thus, these variables were not included in the multivariable model shown in Table 3.4.

Associations with all physician-related characteristics were found. Only one hospital factor was found to influence variation in the number of procedures; hospitals in the top 5% for volume (401 to 577 annual discharges for breast disease) had 31% of women with three or more procedures (OR 1.77, 95% CI

1.07 to 3.81). Similar to the trend observed at the individual level, hospitals with a higher proportion of women living farther than 100 km. were more likely to perform 3 or more diagnostic procedures before surgery (OR 1.70, 95% CI 1.12, 2.57).

## Random Effects

Table 3.5 shows the results of variance components analysis for both outcomes: use of BCS and number of procedures. There were statistically significant variations in the average of proportion of women receiving BCS across hospitals (variance = 0.451, se = 0.079, t=5.71, p<0.0001). These variations were not explained by patient mix, as accounting for women characteristics did not reduce the between-hospital variation (Table 3.5). However, some variation was explained by hospital and surgeon characteristics. Volume and teaching status of the hospital explained 25% of hospital variation not explained by women and surgeons' characteristics (0.25=(0.419-0.314)/0.419). Similarly, there was statistically significant unexplained variation of the average probability of receiving 3 or more procedures across hospitals (variance = 0.566, se = 0.103, t=5.50, p<0.0001). Surgeon's age and number of surgeries performed per year explained 21% of hospital variation while hospital factors explained an additional 10% of this hospital variation. Most of the variation across hospitals was not explained by the study variables, confirming the existence of statistically significant random effects of individual hospitals.

## DISCUSSION

Our results show that in Quebec, the probability of BCS for breast cancer decreased with increasing age, comorbidity, history of breast benign disease, stage of the disease, and the distance to the treating hospital. Similar to other studies<sup>181,197,198</sup>, we found that, although BCS was the treatment of choice for 80% of women, fewer older women were treated with BCS. Whether the identified variation in the rate of BCS reflects variation in quality of care cannot be ascertained, as the optimal percentage of women who should receive BCS is unknown.

Our study also provides evidence that distance to the nearest treating hospital is a determinant of the use of BCS: the rate was 5% lower among women living more than 100 km from a health care center and this difference remained statistically significant after adjusting for other women's characteristics. Lower rates of BCS for women living in remote areas, were also found in the Surveillance, Epidemiology, and End Results (SEER) Program in the United States from 1983 to1986<sup>199</sup>. One potential explanation is that BCS is commonly followed-up by radiotherapy and if there is a lack of access to this specialized care, then mastectomy would become the treatment of choice<sup>16,17</sup>. We found that the increase volume of breast cancer treated in a given hospital was associated with higher proportion of BCS, consistent with the results of other study<sup>181</sup>.

We also found lower rates of BCS among women living in lower income areas and among women treated in hospitals where there was a high proportion of clientele

from more economically disadvantaged areas. Although these two variables are correlated (correlation coefficient 0.54), both were statistically significant even when adjusted for each other, suggesting that they are capturing different constructs. Although the use of aggregate measures of income and education tend to bias the results towards null, we still found effects for these surrogate variables. The association with socio-economic status may reflect the differences in the way treatment options are explained or offered to women from different social backgrounds.

Overall, about 23% of women received three or more procedures before surgery and the percentage increased significantly over time, from 19% in 1992 to 29% in 1997. One explanation for this finding could be that with increasing emphasis on screening, more questionable tumours are being identified <sup>183</sup> and the diagnostic process could be more difficult for these persons. Perhaps as the consequence, the waiting time for breast cancer surgery also increased considerably over this time period in Quebec <sup>183</sup>. Among women who started their episode of care with a biopsy, 46% went on to have a less invasive procedure, such as a bilateral or unilateral mammogram. This may be the result of some women seeking a second opinion, but could also suggest that the biopsy was used prematurely in the diagnostic cycle.

Older physicians tended to use fewer procedures, which may indicate that they are more comfortable using clinical judgement to arrive at a treatment decision. An

unexpected finding was that women from the area more than 100 km from the treating hospital had a greater number of diagnostic procedures than women living nearby. This may have arisen from the desire to make sure of the diagnosis and stage prior to establishing a treatment plan, which would be complicated by having to travel long distances.

The modelling strategy had an important influence on the results of the association between predictors and pattern of care at the hospital and physician level. When analyzed with conventional logistic regression, physician's school of graduation and surgical volume, and hospital volume and teaching status were all significantly associated with pattern of care even after adjusting for woman-level factors. (This comparison is presented in Appendix 3, Table A3.2). However, in hierarchical modelling, these effects lost their statistical significance. Conventional logistic regression ignores clustering and generally causes the standard errors of regression coefficients to be underestimated, thus inflating the statistical significance of the effects. For variables measured at the individual level, the estimates of effect and standard error derived from the hierarchical logistic model did not differ from those derived from conventional logistic regression. Estimates of effect for hospital and surgeon factors were also similar using hierarchical logistic models, but the standard errors were much larger than those were from the conventional models thus, rendering these terms statistically non-significant.

In interpreting these results, it must be remembered that not all variables were measured with as high a degree of precision as would be possible in a clinical study. There was no direct code for tumour stage, instead, it was inferred from specific combinations of diagnostic codes as explained in the methods section. We did not have information on indications or preferences for procedures or treatment, which might be influenced by family history or genetic predisposition. However, it is unlikely that these factors would induce important confounding bias, as there are no reasons to expect their systematic association with the variables considered in this study.

The use of population-based administrative data confers several advantages. Notably, the entire population is represented. Billing accuracy is high as reporting is linked to payment for services rendered and over reporting is monitored through a sophisticated surveillance systems established to investigate potentially fraudulent claims<sup>200</sup>. The accuracy of procedure codes has been verified in other investigation<sup>200,201</sup>.

In conclusion, there was variability in the pattern of care for breast cancer, both in the choice between mastectomy and BCS, and in the type and number of diagnostic procedures preceding surgery. While most women received BCS, the probability depended on several factors more strongly related to the characteristics of the women rather than of the physician or of the hospital. The number of diagnostic procedures before surgery also varied, with almost one-quarter of

women receiving three or more. However, the number of diagnostic procedures tended to be influenced more by physician and hospital. Over the period of this study, the proportion of women receiving three and more diagnostic procedures increased by almost 50%. Whether all these procedures are needed or not is not known and is worthy of investigation. If the number of procedures used continues to increase at the present rate, the health care system may become overloaded.

Characteristics	Number	Percent
Characteristics of women(n=23,370)	· · · ·	
Age (years)		
20-49	7802	33.4
50-64	8095	34.6
65-74	4861	20.8
≥ 75	2612	11.2
Stage of tumour		
Uncertain	154	0.7
Carcinoma in situ	1554	6.6
Localized	14940	63.9
Regional	5824	24.9
Disseminated	898	3.8
Charlson Comorbid Index*		
	21277	91.0
>1	2093	9.0
History of bonign broast discass <sup>=</sup>		
No	20684	88.5
	2686	11.5
Area of residence <sup>§</sup>		
Proximity to hospital		
Less than 100 km	17983	76.9
More than 100 km	5387	23.1
Median household income		
> \$48,100	5945	25.5
\$32,000-\$48,100	11611	49.7
< \$32,000	5814	24.8
Proportion without high school		
< 28%	6351	27.2
28%-50%	10897	46.6
> 50%	6122	26.2
Year of surgery		
1992	3633	15.5
1993	3670	15.7
1994	3846	16.5
1995	3955	16.9
1996	4067	17.4
1997	4199	18.0

Table 3.1. Surgically treated breast cancer in Quebec, 1992-1997: Characteristics of women, the surgeons who performed surgery and the hospitals where the surgery were performed

Table	3.1,	continued.	Surgically	treated	breast	cancer	in	Quebec,	1992-1997:
Chara	cteris	stics of won	nen, the sui	geons w	vho perf	formed s	surg	gery and t	he hospitals
where	the s	surgery wer	e performed	t					

Characteristics	Number	Percent
Characteristics of surgeons (n=724)	·····	
Age of surgeon (years)		
20-44	330	45.6
45-59	266	36.7
≥60	128	17.7
University of graduation		
University of Montreal	218	30.1
Laval University	218	30.1
McGill University	72	9.9
University of Sherbrooke	47	6.5
Other North American universities	40	5.5
Non-North American universities	129	17.8
Number of breast surgeries/ year <sup><math>\Delta</math></sup>		
1-9	585	80.8
10-19	82	11.3
20-39	40	5.5
40-135	17	2.3
Characteristics of hospitals (n=109)		
Number of breast disease discharges /year $^{\Delta}$		
1-100	60	55.0
101-200	24	22.0
201-400	19	17.4
401-577	6	5.5
Teaching status of hospital		
Non-teaching	54	49.9
Teaching or affiliated with university	55	50.1

\*The Charlson comorbidity index was computed one year prior to surgery <sup>193</sup>.

<sup>=</sup> Diagnosed with or had a treatment procedure for benign breast disease in

the 3 year period before surgery.

<sup>§</sup>Quartiles used as cut-points.

 $^{\Delta}$ Cut-points were 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup> and 95<sup>th</sup> percentiles.

Procedures	Number of women (n=23,370)	Percent
Diagnostic procedures during episode* <sup>+</sup>		
Bilateral mammogram	19433	83.2
Unilateral mammogram	2931	12.5
Ultrasound	4297	18.4
Needle biopsy	6534	28.0
Excisional biopsy	3137	13.4
Core biopsy	2329	10.0
Fine needle aspiration	2220	9.5
Number of procedures before surgery <sup>+</sup>		
0	1378	5.9
1	7603	32.5
2	9044	38.7
3	3876	16.6
4	1027	4.4
5	292	1.2
≥6	150	0.7
Surgery		
Breast-conserving surgery	18699	80.0
Mastectomy	4671	20.0

Table 3.2. Procedures performed for women with surgically treated breast cancer in Quebec, 1992-1997

\*At any time and in any order during the episode of breast cancer.

<sup>+</sup>As a woman could have more than one procedure, the sum exceeds the total number of women.

Figure 3.1 First two procedures undergone by women with surgically treated breast cancer in Quebec, 1992-1997



\*Biopsy includes needle biopsy, core biopsy, fine needle aspiration, and excisional biopsy. \*\* Included both unilateral and bilateral

Characteristics	No of BCS	Total no. in the group	% of BCS <sup>#</sup>	Adjusted odds ratio* (95% CI)
Overall use of BCS	18699	23370	80	
Characteristics of Women (n=23,370)				
Woman's age (in five-year grouping) <sup>\$</sup>	18699	23370	80	0.86 (0.85-0.87)
Stage of tumour				
Uncertain	144	154	94	2.81 (1.41-5.60)
Carcinoma in situ	1466	1554	94	3.00 (2.36-3.82)
Localized	12439	14940	83	Referent
Regional	4041	5824	69	0.37 (0.34-0.40)
Disseminated	609	898	68	0.40 (0.33-0.47)
Comorbidity <sup>¤</sup>				
None	17287	21277	81	Referent
At least one comorbid condition	1412	2093	68	0.67 (0.60-0.75)
History of benign breast disease <sup>=</sup>				
No	16553	20684	80	Referent
Yes	2046	2786	76	0.75 (0.66-0.83)
Area of residence				
Proximity to hospital				
< 100 km	14604	17983	81	Referent
≥ 100 km	4095	5387	76	0.77 (0.65-0.92)
Median household income <sup>§</sup>				
> \$48.100	4778	5945	86	Referent
\$32,000-\$48,100	8720	11611	79	0.81 (0.72-0.90)
< \$32,000	5201	5814	76	0.79 (0.70-0.90)
Year of surgery				
1992	2820	3633	78	Referent
1993	2893	3670	79	1.02 (0.91-1.15)
1994	3047	3846	<b>79</b>	1.00 (0.90-1.13)
1995	3210	3955	81	1.11 (0.98-1.25)
1996	3325	4067	82	1.09 (0.97-1.23)
1997	3404	4199	81	1.04 (0.90-1.15)
Characteristics of surgeons <sup>\$</sup>				
Age of surgeon (years)				
20-44	8295	10447	79	Referent
45-59	8422	10423	81	0.94 (0.79-1.12)
≥60	1908	2406	79	0.85 (0.67-1.07)

Table 3.3: Factors associated with the use of breast-conserving surgery in Quebec, 1992-1997

Characteristics	No of BCS	Total no. in	%of	Adjusted
		the group	BCS <sup>#</sup>	odds ratio*
		the Broup	200	(05% CI)
				(95/001)
Number of breast surgeries/year <sup><math>\Delta</math></sup>				
1-9	4747	6177	77	Referent
10-19	4656	5871	79	1.09 (0.91-1.31)
20-39	4279	5329	80	1.08 (0.85-1.36)
40-135	4943	5899	84	1.13 (0.78-1.64)
Characteristics of hospitals <sup>&amp;</sup>				
Number of breast disease				
discharges/year <sup>∆</sup>				
1-100	2457	3398	72	Referent
101-200	2583	3473	74	1.03 (0.69-1.53)
201-400	7124	8984	79	1.24 (0.85-1.81)
401-577	5484	6399	86	1.99 (1.05-3.78)
Teaching status of hospital				
Non-teaching	4588	5990	77	0.85 (0.62-1.16)
Teaching or affiliated to university	13060	16264	80	Referent

Table 3.3, continued. Factors associated with the use of breast-conserving surgery in Quebec, 1992-1997

\* Odds ratios were adjusted for all other variables in the table, CI: confidence interval.

<sup>•</sup>Age in 5-year grouping treated as a continuous variable.

<sup>a</sup> The Charlson comorbidity index was computed one-year prior to surgery <sup>193</sup>.

<sup>=</sup> Diagnosed with or had a treatment procedure for benign breast disease in the 3 year period before surgery.

<sup>\$</sup>94 women had no information on the surgeon.

<sup>&</sup> 1116 women had missing information hospitalization.

<sup>§</sup>Quartiles used as cut-points.

 $^{\Delta}$ Cut-points were 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup> and 95<sup>th</sup> percentiles.

	No. of pro	ocedures		······
Factor	0 (%)	1-2 (%)	≥3 (%)	OR <sup>b</sup> (95% CI)
Overall	6	71	23	······································
Characteristics of Women (n=23,370)				
Age of women (5-year increase)				0.88 (0.87-0.89)
Stage of tumour				
Uncertain	6	70	24	0.71 (0.47-1.09)
Carcinoma in situ	3	68	29	0.96 (0.84-1.09)
Localized	6	71	23	Referent
Regional	5	73	22	0.84 (0.78-0.92)
Disseminated	20	69	11	0.54 (0.42-0.69)
Comorbidity <sup>2</sup>				
None	6	71	23	Referent
At least one comorbid condition	10	73	17	0.95 (0.83-1.10)
History of benign breast disease <sup>■</sup>				
No	5	73	22	Referent
Yes	13	61	28	1.10 (0.98-1.23)
Year of surgery				
1992	8	73	19	Referent
1993	8	73	19	0.95 (0.84-1.08)
1994	6	75	19	0.90 (0.80-1.02)
1995	5	72	23	1.10 (0.97-1.22)
1996	5	69	26	1.19 (1.05-1.35)
1997	5	66	29	1.41 (1.25-1.60)
Areas of residence by postal code Proximity to hospital				
< 100 km	6	73	21	Referent
≥ 100 km	7	66	27	1.28 (1.09-1.51)
Characteristics of surgeons <sup>s</sup>				
Age of Physician (years)				
20-44	5	72	23	1.26 (1.11- 1.48)
45-59	7	70	23	1.14 (1.00-1.31)
≥ 60	10	72	18	Referent
Number of surgeries/year				
1-9	9	72	19	Referent
10-19	5	74	21	1.12 (0.96-1.30)
20-39	5	72	23	1.22 (0.99-1.48)
40-135	4	65	31	1.29 (1.01-1.92)

Table 3.4: Proportions and odds ratios of the number of procedures performed before surgery for women with breast cancer in Quebec, 1992-1997

Table 3.4, continued. Percent distribution and odds ratios of the number of procedures performed before surgery for women with surgically treated breast cancer in Quebec, 1992-1997

	No. of pro	<u></u>		
Factor	0 (%)	1-2 (%)	≥3 (%)	OR <sup>b</sup> (95% CI)
Characteristics of hospitals <sup>&amp;</sup>				
Number of breast disease discharges/ year				
1-100	6	73	21	Referent
101-200	7	76	17	0.99 (0.66-1.46)
201-400	6	73	21	1.04 (0.71-1.53)
401-577	4	65	31	1.77 (1.07-3.81)
Teaching status of hospital				
Non-teaching	7	75	18	Referent
Teaching or affiliated to university	5	70	25	1.24 (0.91-1.70)
% of women residence $\geq 100 \text{km}^{\forall}$				1.71 (1.12-2.57)

<sup>b</sup>ORs are for comparing women had 3 or more procedures to those had 1 or 2

procedures, adjusted for other variables in the model. CI: confidence interval.

<sup>a</sup> The Charlson comorbidity index was computed one-year prior to surgery <sup>193</sup>.

Diagnosed with or had a treatment procedure for benign breast disease in the 3 year period before surgery.

<sup>\$</sup>94 women had no information on the surgeon.

<sup>&</sup> 1116 women had missing information hospitalization.

<sup>∀</sup>Proportion of women who came from the area greater than 100 km.

Effect	Use of I	BCS	Receiving 3 or more diagnostic procedures before surgery		
	Between- hospital variance (SE) <sup>+</sup>	% reduction*	Between- hospital variance	% reduction*	
No independent variables	0.451 (0.079)		0.566 (0.103)		
Only characteristics of woman	0.446 (0.085)	0	0.550 (0.085)	0	
Characteristics of woman and surgeon	0.419 (0.081)	6.1	0.436 (0.086)	20.7	
Characteristics of woman, surgeon, and hospital	0.314 (0.075)	29.6	0.378 (0.074)	31.3	

Table 3.5. Analysis of components of variance for the two outcomes analysed by the hierarchical random effect models

\*The reduction of unexplained variance was calculated by comparing each model to the model to the model that had only characteristics of woman.

\* SE: standard error of estimate of component of variance.

## Chapter 4. Article 2.

#### **Preface to Article 2**

This article addresses the primary study objective, namely, to identify factors that influence the delay in time from receipt of the initial diagnostic procedure to the first definitive surgical treatment among women with localized breast cancer in Quebec between 1992 and 1997. We focused on the biggest group, localized breast cancer, in order to control for confounding by severity of disease.

In order to diminish psychological stress caused by diagnostic uncertainty, clinical practice guidelines for the care and treatment of breast cancer state that the work-up of a breast lump should be completed as rapidly as possible and that long waits to obtain tests should be avoided. Literature regarding determinants of waiting time for care after women entering health care system is sparse. The number of procedures received prior to surgery was the strongest predictor of waiting time, we believe that the number of procedures before surgery is likely an intermediate variable for waiting time. Based on the results of the first article and literature, therefore, a conceptual model of the inter-relationships was formed among factors hypothesized to be related to waiting time (Figure 4.1).

In order to account for clustering effects in this study, we used hierarchical linear regression models to examine the effects of three levels of predictors of waiting time. We examined the validity of applying this statistical methodology in this study by comparing the results with those obtained using conventional linear

regression. A simulation study was also performed as well for this purpose (see Appendix 3 Table A3.1).

# Article 2: Determinants of waiting time from initial diagnostic procedure to surgery among women with localized breast cancer in Quebec, 1992-1997

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#### INTRODUCTION

Screening mammography and regular breast examinations are the principal means for the early detection of breast cancer. It is widely believed that early diagnosis will be effective if treatment can be delivered in a timely fashion<sup>1</sup>. Even though some studies report no adverse impact on survival from delays to treatment<sup>80,99</sup>, others indicate that women with delays in treatment of 3-6 months have lower survival rates<sup>83,85,88,96</sup>. Furthermore, distress is highest while waiting for diagnosis and treatment<sup>67</sup> and, thus, undue delays in treatment can have negative psychological consequences on women and their families<sup>69</sup>. Reducing waiting time will diminish prolonged stress and anxiety and should, therefore, be considered an important component of breast cancer care.

One of the challenges in studying waiting time is that there is no consistency in definitions used. In England, waiting time was defined as the time from a referral by a general practitioner to the first definitive treatment; the median for the period 1997-1998 was 27 days for referrals designated "urgent" and 35 days for "non-urgent" referrals<sup>202</sup>. In Quebec, waiting time was defined as the time to surgery from a breast diagnostic procedure that was considered to have started the episodic of care; the median for the period 1992 to 1998 was 34 days (interquartile range from 19 to 62 days), with 14% of women waiting in excess of 90 days<sup>183</sup>. In a report from Manitoba, waiting time was defined as the time from the last pre-

operative visit with the surgeon until surgery; the median time for 1992-1997 was 16 days<sup>53</sup>.

Understanding the determinants of waiting time to surgery is important in order to develop strategies to shorten delays and thereby improve the clinical and psychosocial outcomes of breast cancer. Provider delay has not been the subject of much research; the few descriptive studies available implied that the lack of surgical manpower and operating room resources were part of the reason for delay<sup>45,51</sup>. Even though specific patient and physician characteristics may influence waiting time at a local level, provider delay is likely to be influenced by the health system in general. The purpose of the present study is to identify the extent to which patient-, physician- and hospital level factors influence the time from the initial breast diagnostic procedure to the first definitive surgical treatment among women with primary breast cancer in Quebec between 1992 and 1997.

## SUBJECTS AND METHODS

## **Sources of Data and Study Population**

The target population was all women 20 years and older, with newly diagnosed and surgically-treated primary breast cancer living in Quebec who were registered with the universal provincial health care insurance plan between 1992 and 1997. The data were derived from physician fee-for-service claims maintained by the
Régie de l'assurance maladie du Québec (RAMQ), the Quebec hospital discharge database, and the 1991 Canadian census.

To identify records of women who were surgically treated for breast cancer, the billing and hospital discharge databases were linked using the unique encrypted medicare number. The diagnosis of primary breast cancer was determined from topography codes, coded according to the International Classification of Diseases, 9<sup>th</sup> revision (ICD-9). These codes are used to identify cancer cases for the purposes of registering tumours in Quebec. Women with primary breast cancer were those with a topography code ICD-9 174.0-174.9, excluding those with codes identifying secondary lymphatic node involvement (196.0-196.9), breast cancer *in situ* (233.0), or metastatic disease (197.0-199.0).

Diagnostic or curative procedures to the breast were identified and extracted from both sources of data. Because the two databases used different systems for coding procedures (the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP) for hospital discharges, versus an internal system [http://www.ramq.gouvqc.ca/pro/pro.html] for RAMQ), the information was reconciled to produce a common classification for mammography, ultrasound, needle and surgical biopsy, lumpectomy, and mastectomy. Although over 94% of surgical records between the two sources of data agreed on procedure and date, leeway was permitted to combine records with minor discrepancies in date and/or type of procedure.

It was usual for women to have multiple breast-related procedures over the study period. Procedures were grouped into "episodes" by combining consecutive procedures that occurred within five months of each other. Because clinical follow-up is often recommended routinely at six-month intervals<sup>192</sup>, a five month period was chosen to reduce the chance of considering a routine follow-up interval as waiting time. The end of an episode was defined as the time of the first definitive surgical treatment. No restriction was placed on the total cumulative time within an episode. Only 2.8% women had more than one episode of care during the index period that included both diagnosis and surgical treatment of breast cancer; in these instances, only the first episode was retained. Although the study index period was from 1992 to 1997, prior (1989-1991) and subsequent (1998) data were used to permit a 3-year window for the identification of previous breast disease and to avoid truncating episodes that spanned administrative time periods, respectively.

# Measurements

Waiting time was defined as the number of days between the date of the first breast-related diagnostic procedure (beginning of episode of breast cancer care) and the date of the first surgery (end of episode).

Information was obtained on three hierarchical levels: the hospital where the surgical treatment was performed, the primary surgeon, and the subject. Information related to the hospital included its teaching status and the annual

average number of discharges for breast-related diseases, including but not limited to breast cancer.

Although women may have consulted with more than one surgeon, the primary surgeon is identified on the database. The following characteristics of this primary surgeon were used in the analysis: the average numbers of breast surgeries performed annually, school of graduation, and age (in 1992). For reasons of confidentiality, the gender of the surgeon was not made available to us by the RAMQ.

Age of subjects were grouped into four categories: 20 to 49, 50 to 64, 65 to 74, and 75 years and older. The Charlson Comorbidity Index was calculated for each woman using the method described by Romano et al. <sup>193</sup>. This index identifies co-morbidity from the 15 secondary ICD-9 diagnoses available on the MedEcho database; the one-year time period before diagnosis was chosen to calculate co-morbidity. In addition to this index, history of benign breast disease in the 3 years before the index episode of care was defined using diagnostic codes (ICD-9: 217.0-217.9, 610.0-610.9) in the MedEcho database and/or procedure codes for the treatment of benign breast disease listed in the RAMQ database (0444, 0594, 1011, and 0821).

We had no direct information on subjects' sociodemographic characteristics. Instead, we used variables from the 1991 Canadian census that were aggregated according to each Canadian six-character postal code. We selected median

household income and the proportion of the population who did not complete high school. As an indicator of access to care, distance from the center of the sixcharacter postal code area of the residence of each subject to the nearest tertiary medical center, mammography center, and acute-care hospital was calculated. After preliminary analysis, distance was categorized as less than 100 km, and greater than 100 km accounting for the access to care<sup>194</sup>. Surgical treatment was classified by type of surgery, whether the surgery was performed at a day-surgery setting or an acute care center; and the year in which the surgery was performed.

#### **Statistical Analyses**

To evaluate factors associated with waiting time, a hierarchical linear regression model was used (MLwiN Software)<sup>196</sup>. Because the data was non-normal (skewed to the right), its natural logarithm was used as the dependent variable in all analysis. The impact of each predictor variable on the natural logarithm of waiting time was evaluated alone, as well as adjusted for other predictors. If exploratory analysis with graphing indicated violation of the linearity assumption, a given continuous predictor was categorized and represented by dummy variables.

The use of hierarchical linear models resolves statistical issues involving nested multi-level data structures. The data were multi-level as more than one woman was treated by the same surgeon, and more than one surgeon practiced in any one hospital. This hierarchy causes the data to be positively correlated, as one would expect that waiting time would be more similar for women treated by the

same surgeon in the same hospital, compared with other women treated by other surgeons and/or in other hospitals. Ignoring such cluster effects violates the fundamental assumption of independence of outcome values required by conventional regression methods. By not accounting for these clusters, the estimated variances of the effects will be underestimated, leading to an inflated probability of a type I error of the significance tests<sup>163</sup>. Hierarchical models can estimate the random effects which account for the variability of waiting time across hospitals (random intercept), and effects of study factors on the variability of waiting time across hospitals (random slope). Thus, to account for the clustering effects in this study, three-level hierarchical models<sup>203</sup> were used to consider simultaneously the association between waiting time for surgery and hospital-, surgeon- and woman-level variables.

The first step of the hierarchical modelling (Appendix) involved partitioning the total variability of log-transformed waiting days into within-surgeon, between-surgeons, within-hospital and between-hospitals components. This was accomplished by fitting a random intercept model, and provided estimates of variance and covariance components. Step 2 involved identifying attributes of the women (woman-level variables) associated with waiting time. This was done by first fitting a series of univariate models, one for each woman-level predictor. Attributes of women retained for inclusion in a multivariable subject-level model were those with p-values lower than 0.15 in the univariate analysis. A non-significant fixed-effect implies that the average effect of a particular woman-level characteristic on the

waiting time is null, and a non-significant random effect implies that the effect is constant across surgeons and hospitals. The third step involved including the effects of factors associated with surgeons (level-2) and hospitals (level 3) on waiting time.

Predictors retained for inclusion in the multivariable between-surgeons and between-hospitals model were required to be significant at the 15% level. However, interaction terms were retained only if significant at the 5% level. For ease of interpretation, percent differences from the median waiting time and corresponding 95% confidence intervals (CI) were calculated for each variable as the exponential of the regression coefficient and its 95% CI.

Even though the number of diagnostic procedures before surgery was the strongest factor associated with waiting time, it was considered to be an intermediate variable on the causal pathway between women's, physician's and hospital's characteristics and waiting time. Therefore, it would not be appropriate to adjust for number of procedures. In a previous paper, factors predicting the number of procedures were explored (see paper 1 in thesis).

#### RESULTS

Overall, a total of 14,940 women who had surgery for breast cancer in the period 1992-1997 were identified. Excluded were women with a previous diagnosis of

breast cancer during the three years prior to the beginning of the index period (1989-1991) (n=234), with chemotherapy prior to surgery (n=359), without a recorded initial diagnostic procedure recorded (n=596), or without hospital discharge information (n=368). A total of 13,383 women with localized primary breast cancer treated by 614 surgeons working in 107 hospitals, were included in analysis.

Table 4.1 shows the distribution of waiting times, from the initial diagnostic procedure to the first definitive surgery, for women with localized breast cancer according to selected characteristics. Overall, the median waiting time was 32 days (interquartile range from 18 to 59 days). The median for this group rose 6 days over this period, from 30 days in 1992 to 36 days in 1997.

Tables 4.2-4.4 provide the results of the sequence of analyses conducted to identify predictors of waiting time (evaluated on a logarithm scale). In the first step, we identified woman-specific factors associated with waiting time. None of the random effects of women's characteristics were significant, indicating that these effects did not vary across hospitals or surgeons. Table 4.2 shows the fixed-effect estimates of women's characteristics (level-1 variables) on the natural logarithm of waiting time, ignoring the clustering effects of surgeons and hospitals. All variables in this table, except for distance to hospital and median household income, met the criteria for inclusion in the multi-variable model (p<0.15).

Table 4.3 shows the results of the univariate regression analyses for hospital- and surgeon-level factors, after adjusting for all selected woman-level factors. All determinants except the annual number of breast surgeries performed by the surgeon were associated with waiting time.

Table 4.4 shows the results of the hierarchical model along with the adjusted percent difference (APD) of median waiting time. For categorical variables, the APD was calculated relative to the reference category; for the one continuous variable, percent of women in the postal code area without high school education, the APD reflected the impact of a 10% change in the proportion without high school. Compared with women younger than 50 years of age, women age 50 to 64 years had the longest waiting time (APD=6.3%, 95% CI: 2.4%, 10.3%), while women 75 years and older had the shortest waiting time (APD=-8.7%, 95%CI: -13.4%, -3.7%). Women with a comorbid condition had a significantly shorter waiting time (APD = -9.0%). However, women with a history of benign breast disease, those who received day-surgery and those who received surgeries in most recent years waited significantly longer. Waiting time was longer among women who were treated by younger surgeons. On average, women who had their surgery performed at a teaching hospital waited 16% (95% CI: 5.1%, 26.9%) longer than those at a non-teaching hospital. The difference in waiting time between teaching and non-teaching hospitals was larger for women who had a mastectomy than for those who had a lumpectomy, as revealed by a statistical significant interaction (p=0.001). The difference in predicted waiting time between

teaching and non-teaching hospitals was four days for lumpectomy and seven days for mastectomy. Essentially, in teaching hospitals, mastectomies took the same amount of time as lumpectomies, it was only in non-teaching hospitals that mastectomies were faster (Figure 4.2).

Table 4.5 shows the estimated random effects from the null model and the final model. There was no statistically significant variability across hospitals or among surgeons in the waiting time for breast cancer surgery. From the null hierarchical model, only 6% of the total variance of the log waiting time was accounted for by the individual hospitals; an additional 4% was explained by individual surgeons. This implies that 90% of the total variance was due to women-level characteristics and unexplained variance. After fitting the three-level hierarchical model, the portion of the 6% between-hospital variance explained by teaching status was 39%. All variables combined reduced the residual variance by 37% (Figure 4.3).

## DISCUSSION

There is limited information about factors associated with waiting time for treatment of breast cancer. Three reviews published in the 1990s<sup>37,104,204</sup> concluded that provider delay was longer when women were younger, non-white, and had non-specific breast symptoms. The studies covered in these reviews were largely descriptive in nature, making it difficult to determine the inter-relationships between factors. Figure 4.1 shows a conceptualization of the inter-relationships

among variables hypothesized to be related to waiting time. The diagnostic process (number of procedures before surgery) is depicted to cross all levels of variables and is most likely an intermediate variable for waiting time. We noted previously, that the number of procedures before surgery was key to explaining waiting time<sup>183</sup>. Number of procedures and type of surgery were variables considered as part of the pattern of care. A previous study in this series explored factors contributing to pattern of care and identified again, the importance of women-level factors but also a significant random variation across hospitals and across surgeons (see paper 1 in thesis).

Waiting time was defined as the time from the first diagnostic procedure to the first definitive surgery, and probably reflects mostly provider delay<sup>204</sup>. In four studies, younger women were found to have longer waiting times<sup>15,48,129,131</sup>. Younger women may be more difficult to diagnose because of the high incidence of benign breast disease and the high density of mammary tissue on radiographic images. We found a non-linear relationship between age and waiting time: women younger than 50 years and those 75 years and older had shorter waiting times. Even though we limited our study to women with primary localized breast cancer, this association between waiting time and age may be due to younger women having larger or more aggressive tumours that are in urgent need of surgery. Oldest women are more likely to receive a mastectomy after less investigation, and thus, experience shorter waiting times. It should be noted, however, that the largest

group of women with breast cancer have localized disease at time of diagnosis and are aged between 50 and 75 years.

Co-morbidity and history of benign breast disease are important factors affecting physicians' decisions about caring for breast cancer. We found that women with at least one comorbid condition progressed to surgery faster than did women who had no comorbid conditions. This may be partly because healthier women are less likely to have regular contact with physicians. They would be less well known to the physician at the time of presentation and, thus, the diagnostic work-up may take longer.

Our results showed that waiting time for breast cancer surgery was not determined by income status. Similarly, Benk et al.<sup>55</sup> found that women living in Montreal with breast cancer who had lower incomes did not wait longer for their radiation treatment post-surgery than did higher income patients. This may be a result of the Canadian universal medicare system which, in principal, provides equal access to health care. However, we found lower education was related to longer waiting times, suggesting that these women have more difficulty navigating through a complex health care system and, thereby, accumulate delays at a variety of points.

Women who had their surgery performed by surgeons 50 years and older had a shorter waiting time than did women who were cared for by younger surgeons. Older physicians tended to use fewer procedures<sup>205</sup>, which may indicate that they

are more comfortable using clinical judgements to arrive at a treatment decision. The variation of waiting time across medical school of graduation may be a reflection of preference of surgeon's practice patterns.

Hospital size, volume, and affiliation with a medical school are factors that have been found to be related to the pattern of care received by breast cancer patients<sup>132,150,205</sup>. We found evidence that women treated in teaching hospitals had significantly longer waiting times for breast cancer surgery than those treated in non-teaching hospitals. We also found that the increased number of hospital discharges each year for breast-related disease was a risk factor for longer waiting times. Benk et al. also found longer delays to radiotherapy post-surgery for patients treated in teaching hospitals<sup>55</sup>. Teaching hospitals have higher patient volumes and may also have more complicated cases to manage. The interaction between teaching status of hospital and type of surgery performed indicates an even greater disparity in waiting time between teaching and non-teaching hospitals among women who received mastectomies. In teaching hospitals, mastectomies took as long as lumpectomies but, in non-teaching hospitals, the waiting time to mastectomy was shorter than lumpectomy. This likely reflects a resource issue in large, teaching hospitals.

Mayo et al., noted that waiting time for breast cancer surgery increased by 37% in Quebec from 1992 to 1998. Coincidentally, there was a reduction in health care spending over this period that accentuated in the latter years where the most

dramatic increases were observed<sup>183</sup>. The hardest hit were in-patient resources including operating rooms and beds.

The use of administrative databases to investigate waiting time has a number of advantages. Notably, the entire population is covered and billing accuracy is high as reporting is linked to payment for services rendered<sup>200,201</sup>. However, these databases lack in detail regarding size of tumour, receptor status, genetic profile, family history, and behavioural factors that might explain treatment delay. These factors undoubtedly will explain a proportion of 60% of variance unexplained by variables included in the three-level hierarchical model.

Large proportion of variability in waiting time was explained by women's characteristics such as age (mid-range had longer waiting time), comorbidity, history of benign breast disease, education level. Apart from identifying high risk individuals or groups, these factors help us understand how delays arise. It would be of interest to explore further the role of education or lack of education in increasing waiting time. Do the delays arise because of difficulty that the women experience in working with the system, or does the system behave differently with different groups of people? Knowing that education is a factor may help in identifying how to communicate more effectively with all segments of the population.

Finally, there was no statistically significant variation of waiting time across hospitals and surgeons. This implies that the observed waiting times, which might

be considered long in the eyes of some people, is not concentrated in only a few hospitals or surgeons but widespread. Therefore, to reduce overall waiting time, strategies would need to be systematically applied. Possible solutions are increasing the co-ordination of care so all breast cancer services are offered in one setting and overseen in a consistent manner. Unexpectedly long delays could be flagged for intervention. The use of administrative data and the hierarchical modeling strategy are innovative ways of examining this complex problem and suggests that the solutions will be complex. Table 4.1. Waiting time from the first diagnostic procedure to the first surgery for women with localized breast cancer, according to women-, surgeon-, and hospital-related characteristics, Quebec 1992-1997

Characteristics of woman, surgeon and hospital	Number	Percent	Median waiting time in days (interquartile range)		
Overall	13383	100.0	32 (18-59)		
Characteristics of subjects (n=13,383)					
Age (years)					
20-49	4081	30.5	32 (19-61)		
50-64	4782	35.7	34 (20-63)		
65-74	2985	22.3	32 (17-55)		
> 75	1535	11.5	28 (15-52)		
Charlson comorbidity index*					
0	12221	91.3	33 (19-59)		
>1	1162	8.7	28 (15-49)		
History of benion breast disease <sup>=</sup>					
No	11992	89.6	32 (18-56)		
Yes	1391	10.4	40 (22-76)		
Area of residence <sup>§</sup>	1071	1011			
Proximity to hospital					
< 100  km	10316	77 1	34 (19-59)		
> 100  km	3067	22.9	29 (16-52)		
Median household income in the subject's postal code area (\$CAN) > \$48,000 \$32,000-\$48,000 < \$32,000	3216 6281 3886	24.0 47.0 29.0	32 (18-57) 33 (18-59) 32 (18-57)		
Proportion without high school education in the subject's postal code area					
<28%	3602	26.9	31 (17-54)		
28-50%	6276	46.9	32 (18-58)		
>50%	3505	26.2	33 (19-59)		
Type of surgery					
Breast conserving surgery	11151	83.3	33 (19-59)		
Mastectomy	2232	16.7	28 (15-50)		
Number of procedure before surgery					
1	4468	33.4	24 (14-41)		
2	5576	41.7	31 (18-53)		
3	2445	18.3	47 (26-81)		
4	622	4.6	70 (41-114)		
≥5	272	2.0	109 (59-282)		

Table 4.1. Waiting time from the first diagnostic procedure to the first surgery for women with localized breast cancer, according to women-, surgeon-, and hospital-related characteristics, Quebec 1992-1997

Characteristics of woman, surgeon and hospital	Number	Percent	Median waiting time in days (interquartile range)
Surgical setting			
Acute care	9566	71.5	30 (17-55)
Day-surgery	3817	28.5	35 (20-64)
Year of surgery			
1992	1973	14.7	29 (15-57)
1993	2051	15.3	30 (17-57)
1994	2205	16.5	28 (16-51)
1995	2290	17.1	32 (18-57)
1996	2388	17.8	34 (20-60)
1997	2476	18.5	37 (22-65)
Characteristics of surgeons (n=614) Age (years)			
20-49	353	57.5	33 (19-58)
50-64	216	35.2	31 (17-56)
≥ 65	45	7.3	28 (16-55)
University of graduation			
Montreal University	184	30.0	35 (21-65)
Laval University	179	29.2	29 (16-55)
McGill University	65	10.6	28 (16-51)
University of Sherbrooke	44	7.2	33 (18-58)
Other North American Universities	26	4.2	35 (19-68)
Outside North American Universities	116	18.9	29 (16-51)
Number of breast surgeries per year**			
1-9	475	77.4	30 (16-55)
10-19	82	13.4	28 (15-49)
20-39	40	6.5	32 (18-57)
40-135	17	2.8	38 (23-68)
Characteristics of hospitals (n=107)			
Number of breast disease discharges per year**			
1-95	71	66.4	29 (16-52)
96-171	19	17.8	28 (15-51)
172-397	12	11.2	34 (19-60)
398-577	5	4.7	38 (22-67)
Teaching or affiliated to a university			
No	52	48.6	28 (15-51)
Yes	55	51.4	35 (21-62)

\*Charlson comorbidity index within one year prior to surgery <sup>193</sup>.

<sup>=</sup> Diagnosed with or had a treatment for benign breast disease during the 3 years prior to the surgery.

<sup>§</sup> Cut-points for median household income and proportion without high school were the 25<sup>th</sup> and 75<sup>th</sup> percentiles.

\*\*Cut-points were the 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, and 95<sup>th</sup> percentiles.

Characteristics	Difference of	95% confidence
	median waiting	intorval (P/)
	time relative to	interval (%)
	reference <sup>∀</sup> (%)	
Age (years)		
20-49	Reference	
50-64	4.3	0.5, 8.2
65-74	-6.0	-9.8, -2.1
≥75	-14.0	-18.3, -9.5
Charlson comorbidity index*		
=0	Reference	
≥1	-15.8	-20.3, -11.1
History of hanian breast disease <sup>=</sup>		
No history	Reference	
Having history	22.3	16 4 28 4
Having history	22.0	10.4, 20.4
Area of residence		
Proximity to hospital		
<100 km	Reference	
≥100 km	-4.8	-10.6, 2.4
		,
Median household income in the subject's postal	-0.1	-0.3, 0.1
code area		
Proportion without high school education in the	1.6	-0.2, 3.7
subject's postal code area (per 10% increase)		
Type of surgery		
Lumpectomy	Reference	
Mastectomy	-10.3	-14.8, -5.6
Number of procedure before surgery		
1	Reference	
1		38 5 48 0
2	108.3	99.0 117.1
4	208.9	188 5 230 9
>5	389.4	342.8, 440.8
Sumary cotting	00711	0.210, 1.010
A cute care	Poforonco	
Dav-surgery	20 2	160 280
	22.0	10.0, 20.9

Table 4.2. Unadjusted fixed-effect estimates of the logarithm waiting time by selected characteristics of women ignoring clustering effects of surgeons or hospitals

Table 4.2, continued. Unadjusted fixed-effect estimates of the logarithm waiting time by selected characteristics of women ignoring clustering effects of surgeons or hospitals

Characteristics	Difference of median waiting time relative to reference <sup>∀</sup> (%)	95% confidence interval (%)	
Year of surgery	······································		
1992	Reference		
1993	5.0	-0.6, 10.9	
1994	-3.1	-8.1, 2.1	
1995	6.2	0.7, 12.0	
1996	15.1	9.4, 21.2	
1997	26.2	20.0, 32.8	

<sup>V</sup>Percent difference of median calculated as [exp(coefficient from hierarchical linear regression analysis of natural logarithm of waiting time)-1]\*100

\*Charlson comorbidity index within one year prior to surgery <sup>193</sup>.

<sup>=</sup> Diagnosed with or had a treatment for benign breast disease during the 3 years prior to the surgery.

Table	4.3.	Fixed-effect	estimates	of	logarithm	waiting	time	by	select	ed
charac	teristic	cs of surgeor	ns, and hos	spita	ls, adjustin	g only fo	or cha	racte	eristics	of
womer	1									

Characteristics	Difference of	95% confidence		
median waiting time relative to reference∀ (%)		interval (%)		
Characteristics of surgeon (n=614)		<u></u>		
Age of physician (years)				
20-49	Reference			
50-64	-6.9	-12.3, -1.0		
≥65	-6.6	-16.8, 4.9		
University of graduation				
Montreal University	Reference			
Laval University	-10.7	-17.6, -3.2		
McGill University	-6.4	-16.0, 4.3		
University of Sherbrooke	-2.6	-13.0, 9.2		
Other North American Universities	6.0	-9.4, 24.0		
Outside North American Universities	-9.9	-17.2, -2.0		
Number of breast surgeries per year**				
1-9	Reference			
10-19	-4.3	-10.1, 1.9		
20-39	5.7	-2.3, 14.3		
40-135	7.5	-4.3, 20.6		
Characteristics of hospitals (n=107)				
Number of breast disease discharges per year**				
1-95	Reference			
96-171	-6.8	-17.4, 5.3		
172-397	12.7	-2.1, 29.8		
398-577	26.7	3.8, 54.8		
Non-teaching	Reference			
Teaching or affiliated to a university	14.6	3.5, 26.9		

<sup>V</sup>Percent difference of median calculated as [exp(coefficient from hierarchical linear regression analysis of natural logarithm of waiting time)-1]\*100. Adjusted for woman-level characteristics: age, comorbidity, history of benign breast disease, education level in area of subject's residence, type of surgery, surgical setting and year the surgery performed.

\*\*Cut-points were the 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, and 95<sup>th</sup> percentiles.

Table 4.4. Results of multivariable analysis of the determinants of logarithmic waiting time from the first diagnostic procedure to surgery for women with localized breast cancer in Quebec, 1992-1997

Characteristics of woman, surgeon, and hospital	Median waiting time	Adjusted difference of median waiting time relative to reference $\forall$			
Fixed effects	(days)	% difference	95% confidence interval (%)		
Characteristics of subjects (n=13,383)					
Subject's age (years)					
20-49	32	Referent			
50-64	34	6.3	2.4, 10.3		
65-74	32	-1.4	-5.4, 2.8		
≥ 75	28	-8.7	-13.4, -3.7		
Comorbidity*					
None	33	Referent			
At least one comorbid condition	28	-9.0	-13.8, -3.8		
TT' ( C1 ' 1 ( 1' =					
History of benign breast disease	22	Deferent			
NO Var	32		117 265		
	40	20.4	14.7, 20.5		
Proportion without high school education in the		0.5			
subject's postal code area (per 10% increase)	33	2.5	0.7, 4.4		
Type of surgery					
Breast conserving surgery	33	Referent			
Mastectomy	28	-3.6	-9.0. 2.0		
			,		
Surgery setting	•				
Acute care	30	Referent	10 < 10 0		
Day-surgery	35	14.8	10.6, 19.2		
Year of surgery					
1992	29	Referent			
1993	30	5.2	-0.4, 11.2		
1994	28	-2.5	-7.5, 2.8		
1995	32	6.4	0.9, 12.2		
1996	34	14.1	8.4, 20.1		
1997	37	24.9	18.7. 31.4		
		,	,		

Table 4.4. Results of multivariable analysis of the determinants of logarithmic waiting time from the first diagnostic procedure to surgery for women with localized breast cancer in Quebec, 1992-1997

Characteristics of woman, surgeon, an hospital	d Media waiting t	n Adjusted dif ime waiting t ref	ference of median time relative to ference <sup>∀</sup>		
Fixed effects	(days)	% difference	95% confidence interval (%)		
Characteristics of surgeons (n=614)					
Physician age (years)					
20-49	33	Referent			
50-64	31	-6.3	-11.8, -0.4		
≥65	28	-4.3	-14.9, 7.6		
University graduated from					
Montreal	35	Referent			
Laval	29	-10.2	-17.2, -2.7		
McGill	28	-8.3	-17.7, 2.1		
Sherbrooke	33	-4.0	-14.2, 7.5		
North American	35	7.1	-8.4, 25.2		
Outside North American	29	-8.9	-16.2, -0.9		
Characteristics of hospitals (n=107)					
Teaching or affiliated to a university					
No	28	Referent			
Yes	35	15.5	5.1, 26.9		
<sup>∀</sup> Percent difference of median	calculated as [	exp(coefficient fi	rom hierarchical		

linear regression analysis of natural logarithm of waiting time)-1]\*100

\*Charlson comorbidity index one year prior to surgery <sup>193</sup>.

<sup>=</sup> Diagnosed with or had a treatment procedure for benign breast disease within 3 years prior to the surgery.

	Null n	nodel*	Full n	nodel**
Fixed effect	Coefficient	S.E.	Coefficient	S.E.
Overall mean log of	3.362	0.027	3.112	0.056
waiting time				
Random effects	Variance component	Proportion of total variation (%)	Variance component	% of reduction compared to null model
Between-hospital variance*	0.049	6	0.030	39
Between-surgeon variance#	0.031	4	0.029	6
Residual	0.755	90	0.474	37

# Table 4.5. Analysis of variance with random effects

\*Intercept model without covariates

\*\*Variables included in the table 4.4

\*Not statistically significant at 5% level by likelihood ratio test



Figure 4.1. Conceptual model for determinates of waiting time for breast cancer surgery



Figure 4.2. Effect of hospital teaching status on waiting time by type of surgery



No statistically significant variation of waiting time between hospitals



# **Chapter 5. Article3**

# **Preface to Article 3**

The purpose of this thesis project is to study health care services for the detection, diagnosis and treatment of breast cancer in order to illuminate areas of improvement for providing better outcomes. The objective of this article is to estimate the impact of prior mammography on the stage of breast cancer at diagnosis in the general population.

In the two previous articles, we identified the risk factors of the delay for diagnosis and treatment. Here, we would like to use existing administrative data to examine whether mammography before the episode of breast cancer is associated with an earlier stage of disease. This information would be useful for the overall process of care of breast cancer, including pre-clinical detection, diagnosis and treatment.

# Article 3. Prior Use of Mammography Protects against Late-Stage Breast Cancer: A Population Based View of Screening Effectiveness

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#### INTRODUCTION

Randomized clinical trials have shown that screening mammography leads to a 20% to 40% reduction in mortality from breast cancer<sup>206-212</sup>. Although the additional benefits of an annual screening mammogram over clinical breast examination alone have been challenged<sup>213,214</sup>, at least 22 countries have organized screening mammography programs for women 50 years and older<sup>215</sup>. The expectation is that the implementation of these programs on a population basis will reduce mortality from breast cancer. For this benefit to have a similar impact at the population level, the program has to be widely subscribed to and it has to be as effective as found in the experimental trials.

According to a 1996 report on mammography screening programs in eight Canadian provinces among women age 50-69 years, estimated participation rates varied from 11% to 54% across the provinces<sup>216</sup>. Quebec has one of the highest mortality rates for breast cancer in Canada. In 1997, the age-standardized mortality rate for breast cancer was 29 per 100,000 for women of all ages and 76 per 100,000 for women age 50 to 64. Both these rates were higher than the overall Canadian rate [http://www.cancer.ca/stats2000/tables/tab6e.htm]. Until 1998, it also had no organized screening program. The presence at diagnosis of metastases in the lymphatic nodes or in more distal anatomical sites is the most significant determinant of survival<sup>217-219</sup> and screening reduces mortality by allowing a quicker detection of such metastases. Demonstrating a lower

proportion of late-stage disease in the general population in a non-experimental setting would bolster the "credibility" that screening by mammography is an effective method for reducing overall mortality. The purpose of this study, therefore, is to estimate in the general population the impact of mammography on the stage of presentation of breast cancer.

# METHODS

#### Data source and study population

The target population was all women 20 years and older newly diagnosed with breast cancer, living in Quebec between 1992 and 1997 and registered for the provincial health care insurance plan. The data for this study came from physician fee-for-service claims maintained by the Régie de l'assurance maladie du Québec (RAMQ), the Quebec hospital discharge database (MedEcho), and the 1991 Canadian census.

From the MedEcho, records of women with a diagnosis of breast cancer and breast carcinoma in situ, classified according to the Ninth Revision of the International Classification of Diseases (ICD-9 174.0-174.9, 233.0, 238.3) were extracted. Also identified were records with a diagnostic code for secondary lymph node involvement (ICD-9 196.0-196.9) or metastatic disease (ICD-9 197.0-199.0) when a prior diagnosis of breast cancer was found. In the index period 1992 to 1997, a total of 24,114 women with a newly diagnosed breast cancer were thus identified. Excluded were women with a breast neoplasm of uncertain

behavior (ICD-9 238.3, n=254) and women with a previous diagnosis of breast cancer before the index period (n=644).

The RAMQ billing data base was used to identify any records for diagnostic or curative procedures related to breast during the index period (1992 – 1997). Additional data obtained for the period 1989 to 1992 permitted a 3-year window to identify previous breast-related procedures and other disease.

The RAMQ and the MedEcho databases were linked through a unique encrypted personal identifier. For any one woman, breast-related procedures were identified from the physician service claim data and were grouped into an "episode" by combining as a single series those consecutive procedures that were performed within 5 months of each other. The five-month interval was chosen to avoid combining procedures for routine follow-up commonly recommended at six-month intervals<sup>192</sup>. No restriction was placed on the cumulative duration of an episode, and only episodes that included a diagnosis of breast cancer were retained for analysis.

#### Measures

The outcome variable for this study was stage at diagnosis. Using the MedEcho ICD-9 diagnostic codes, tumours diagnosed as carcinoma in situ and primary breast cancer without lymphatic node involvement were classified as "early-stage" disease, while those diagnosed as a primary breast cancer with lymphatic node involvement or with disseminated cancer were classified as "late-stage" disease.

Bilateral mammography examinations were identified from the RAMQ billing claims (procedure codes 8141, 8143, 8145, 8147, 8049, 8071, 8079) in the two and a half years before the episode that led to a diagnosis of breast cancer. For the purpose of confidentiality, the RAMQ provided age in five-year groups. As most screening mammography programs target women 50 to 69 years old, we regrouped age into three categories (20-49, 50-69, ≥70 years). The Charlson Comorbidity Index was calculated for each woman using the method described by Romano et al.<sup>193</sup>. This index identifies co-morbidity from the 15 secondary ICD-9 diagnoses available on the MedEcho database; the one year time period before diagnosis was chosen to calculate co-morbidity. History of benign breast disease was derived both from the diagnostic codes in the MedEcho database (ICD-9 217.0-217.9, 610.0-610.9) and from procedure codes for treatment of benign breast disease as recorded in the RAMQ database (0444, 0594, 1011, 1172, 1175). A minimum time window of three years preceding the episode under consideration was used to identify this history.

We had no direct information on socio-economic status. Instead, we created surrogate variables by linking each subject's 6-character postal code to the 1991 Canadian Census. The median household income and the proportion of the population who did not complete high school in each woman's postal code area of residence were calculated. The distance from each woman's place of residence to the nearest tertiary medical center, mammography center, and acute-care hospital was also calculated and used as a proxy for access to care<sup>194</sup>.

# **Statistical Analysis**

The association between prior bilateral mammography and stage was estimated using logistic regression. Separate analyses were carried out according to history of benign breast disease and age group. We estimated odds ratios for late-stage versus early-stage disease comparing women who underwent at least one bilateral mammography during 30 months before the episode to women who did not have a mammogram. Logistic models that adjusted for age, comorbidity, year of diagnosis of breast cancer, distance to hospital, median household income and education level in the woman's resident area were developed. For models within each age group, additional adjustment was made for age to account for any residual confounding effects. These associations were also evaluated for different subgroups of women defined by values of the covariates.

#### RESULTS

Table 5.1 shows the characteristics of the 23,216 women diagnosed with breast cancer by age. Forty six percent of women were between 50 and 69 years of age and 21% of women were 70 years and older. The proportion of women with co-morbidity increased with age: 3% among women 20 to 49 years old and 19% among those 70 years and older. Overall, 79% of women started their episode of care with a bilateral mammography. Table 5.2 presents the frequency distribution of women who had prior mammograms in the 30 months preceding the episode of breast cancer. On average, 13.7% of women with breast cancer had a

mammogram in this period. Women younger than 70 years of age were twice as likely to have had a prior mammogram than women over 70 years of age (15% vs. 7%). Forty percent of women with a history of benign breast disease had a prior mammogram, compared with 12% of women without such a history. Women with other comorbid conditions, those living more than 100 km from a health care center, and those living in an area where the population had a lower education were less likely to have had prior mammograms.

Overall, 29% of women were classified as having a diagnosis of late-stage breast cancer (Table 5.3). Younger women, those with at least one comorbid condition, and those without a history of benign breast disease were more likely to have late-stage tumours. The proportion of late-stage disease decreased over time. Distance to health center, median household income, and level of education were not associated with late-stage disease.

The risk of presenting with late-stage breast cancer was lower in women with prior mammography as compared with women who had none: OR 0.61 (95%CI: 0.56-0.67). Table 5.4 shows that the association did not vary appreciably by history of benign breast disease and age. Figure 1 shows the difference in the proportion of women with late-stage cancer according to whether they had had a mammogram in the preceding 30 months. The difference in proportion varied from 9% for women between the age of 50 to 69 years to 13% for women 70 years and older. For women without history of benign breast disease, after adjusting for age,

comorbidity and year of diagnosis of breast cancer, the association between having a mammogram and late-stage of disease was statistically significant for all age groups (OR=0.42-0.62). For women with a history of benign breast disease, the protective effect of prior mammography was significant only in the largest subgroup (women age 50-69).

## DISCUSSION

This study provides evidence of the benefit of prior bilateral mammography for reducing the probability of detecting breast cancer at a late stage. In addition, the benefit of mammography to reduce the probability of late stage was similar to the findings in the clinical trial<sup>220</sup>, a 39% reduction in late-stage breast cancer among women between 50 and 69 years of age. Clinical trials are often criticized for including only a selected group of subjects, which presumably limits the generalizability of the findings. In addition, the patterns of care used in the experimental situations are usually optimal. As the results of these two features, when applied to the general population, the benefits are often less than that observed in the trials. The results of our study support the benefits of screening for breast cancer and indicate that if screening is applied widely, there would be a considerable benefit to the general population.

To illustrate this benefit assume that the five-year case-fatality rate of women with late-stage breast cancer is 60% and that of women with early-stage disease is

 $10\%^{221,222}$ . In our study, nearly 30% of all breast cancer cases were diagnosed as late-stage tumours. If all our subjects had had a screening mammogram, then the 30% of women with late-stage disease would have been reduced by 39%, yielding a new prevalence of late-stage diagnosis of 18.3% ( $30\% \times (100\%-39\%)$ ). Prior to full screening, the expected number of deaths per 100 persons with late-stage cancer is 60% of 30 (18 women). With full screening, the number of women presenting with late-stage cancer would be reduced to 18.3 out of 100 and the number of deaths among this group would be 11.0 ( $60\% \times 18.3$ ). This equates to a reduction in mortality of 39% ((18-11)/18).

The earlier detection of breast cancer by mammography was also observed for women outside of the recommended screening age group (50 to 69 years). In fact, the benefit for women age 70 years and more was larger than for the 50-69 year group (OR 0.42 versus 0.61). Other observational studies have reported a similar benefit of regular mammography in older women<sup>209,223</sup>.

The observed beneficial effect of mammography is not a result of over-detection of borderline breast cancer as we excluded women with neoplasm of uncertain behaviour. Furthermore, the results are unchanged by removing cases of *carcinoma in situ* that should progress slowly. Our definition of stage was derived from diagnostic codes recorded on the hospital discharge database. There may be some inaccuracies in diagnostic coding, but this should be independent of prior mammography. Thus, any misclassification should be non-differential and thereby
attenuating the strength of the association between prior mammography and stage at diagnosis.

These data do not distinguish a screening from a diagnostic-mammography, or from follow-up mammography among women already treated for breast cancer or Despite the potential for missing some other types of breast disease. mammograms carried out at private clinics, the rate of regular mammography use found in this study (13.7%) is compatible with data from various Quebec sources. Data from provincial health records indicate that, in 1991, some 348,000 carried out 323.000 women mammograms were on {http://www.ramq.gouv.qc.ca/sta/rpsta.htm}. The number of women in Quebec between the ages of 25 and 75 is estimated at approximately 2.2 million. Thus, only about 14.7% of all women in this age range would have a mammogram in any Prior mammography in this study was defined as having had at least one vear. bilateral mammogram within the 2-year period before the initial procedure of the episode of breast cancer care. However, 79% of women started their episode of care with a bilateral mammogram and thus, the 13.7% may represent regular users of mammogram.

In conclusion, we found that regular use of mammography was associated with a higher probability of detecting breast cancer at an earlier stage, in agreement with data from randomized clinical trials. Evidence is added to support the development and maintenance of organized screening programs.

	Age				
	20 to 49	50 to 69	≥ 70	Total	
	N (%)	N (%)	N (%)	N (%)	
Overall	7719	10728	4769	23216	
Start episode with					
Bilateral mammography	6011 (78)	8815 (82)	3370 (71)	18196 (79)	
Other procedure	1708 (22)	1913 (18)	1399 (29)	5020 (21)	
Comorbidity*					
None	7529 (97)	9714 (90)	3888 (81)	21131 (91)	
At least one comorbid condition	190 (3)	1014 (10)	881 (19)	2085 (9)	
History of benign breast disease					
No	6580 (85)	9560 (89)	4428 (93)	20568 (89)	
Yes	1139 (15)	1168 (11)	341 (7)	2648 (11)	
Area of residence					
Proximity to hospital					
< 100 km	5927 (77)	8233 (77)	3713 (78)	17873 (77)	
≥ 100 km	1792 (23)	2495 (23)	1056 (22)	5343 (23)	
Median household income <sup>§</sup>					
≥ \$32.000	6029 (78)	7628 (71)	2842 (60)	16499 (71)	
< \$32,000	1690 (22)	3100 (29)	1927 (40)	6717 (29)	
Proportion without high school <sup>§</sup>					
< 50%	6038 (78)	7744 (72)	3350 (70)	17132 (74)	
≥ 50%	1681 (22)	2984 (28)	1419 (30)	6084 (26)	
Year of breast cancer diagnosis					
1992	972 (13)	1652 (15)	989 (21)	3613 (16)	
1993	1093 (14)	1700 (16)	847 (19)	3640 (16)	
1994	1216 (16)	1801 (17)	795 (17)	3812 (16)	
1995	1336 (17)	1820 (17)	774 (16)	3930 (17)	
1996	1479 (19)	1867 (17)	699 (15)	4045 (17)	
1997	1623 (21)	1888 (18)	665 (14)	4176 (18)	

Table 5.1. Characteristics of women with newly diagnosed breast cancer, according to age, Quebec, 1992-1997

\*Charlson comorbidity index calculated one year prior to the diagnosis of breast cancer <sup>193</sup>.

<sup>=</sup> Diagnosed as benign breast disease within 3 years before the diagnosis of breast cancer.

Characteristic	Age 20-49 No. (%)	Age 50-69 No. (%)	Age≥70 No. (%)	
Overall	1051 (13.6)	1797 (16.8)	333 (7.0)	
Comorbidity*				
None	1026 (13.6)	1676 (17.3)	297 (7.6)	
At least one comorbid condition	25 (13.2)	121 (11.9)	36 (4.1)	
History of benign breast disease <sup>■</sup>				
No	576 (8.8)	1249 (13.1)	227 (5.1)	
Yes	475 (41.7)	548 (46.9)	106 (31.1)	
Area of residence <sup>§</sup>				
Proximity to hospital				
< 100 km	828 (14.0)	1436 (17.4)	280 (7.5)	
≥100 km	223 (12.4)	361 (14.5)	53 (5.0)	
Median household income <sup>§</sup>				
≥ \$32,000	827 (13.7)	1336 (17.5)	193 (6.8)	
< \$32,000	224 (13.3)	461 (14.9)	140 (7.3)	
Proportion without high school <sup>§</sup>				
< 50%	839 (13.9)	1388 (17.9)	261 (7.8)	
≥ 50%	212 (12.6)	409 (13.7)	72 (5.1)	
Year of breast cancer diagnosis				
1992	135 (13.9)	279 (16.9)	69 (7.0)	
1993	150 (13.7)	330 (19.4)	61 (7.2)	
1994	168 (13.8)	320 (17.8)	80 (10.1)	
1995	180 (13.5)	303 (167)	49 (6 3)	
1996	192 (13.0)	290 (15.5)	39 (5 6)	
1997	226 (13.9)	275 (14.6)	35 (5.3)	

Table 5.2. Prior mammography in two years before the episode of care, by selected characteristics and age

\*Charlson comorbidity index calculated one year prior to the diagnosis of breast cancer <sup>193</sup>.

<sup>=</sup> Diagnosed with a benign breast disease within 3 years before the diagnosis of breast cancer.

Characteristic	Age 20-49	Age 50-69	Age≥70
	No. (%)	No. (%)	No. (%)
Overall	2532 (32)	2991 (28)	1226 (25)
Comorbidity*			
None	2449 (33)	2636 (27)	936 (24)
At least one comorbid condition	83(44)	355 (35)	263 (30)
History of benign breast disease <sup>™</sup>			
No	2201 (33)	2721 (28)	1120 (25)
Yes	331 (29)	270 (23)	79 (23)
Areas of residence <sup>§</sup>			
Proximity to hospital			
Less than 100 km	1976 (33)	2278 (28)	929 (25)
More than 100 km	556 (31)	713 (29)	270 (26)
Median household income <sup>§</sup>			
Greater than \$32,000	1995 (33)	2106 (28)	723 (25)
Less than \$32,000	537 (32)	885 (29)	476 (25)
Proportion without high school <sup>§</sup>			
Less than 50%	1971 (33)	2128 (27)	826 (25)
Greater than 50%	561 (33)	863 (29)	373 (26)
Year of breast cancer diagnosis			
1992	348 (36)	514 (31)	288 (29)
1993	371 (34)	489 (29)	218 (26)
1994	420 (35)	515 (29)	198 (25)
1995	453 (34)	494 (27)	194 (25)
1996	431 (29)	520 (29)	156 (22)
1997	509 (31)	459 (24)	145 (22)

Table 5.3. Proportion of late-stage disease by selected characteristics and age

\*Charlson comorbidity index calculated one year prior to the diagnosis of breast cancer <sup>193</sup>.

<sup>=</sup> Diagnosed with a benign breast disease within 3 years before the diagnosis of breast cancer.

Characteristic	Age 20-49	Age 50-69	Age≥70	
	No. (%)	No. (%)	No. (%)	
Overall	2532 (32)	2991 (28)	1226 (25)	
Comorbidity*				
None	2449 (33)	2636 (27)	936 (24)	
At least one comorbid condition	83(44)	355 (35)	263 (30)	
History of benign breast disease <sup>=</sup>				
No	2201 (33)	2721 (28)	1120 (25)	
Yes	331 (29)	270 (23)	79 (23)	
Areas of residence <sup>§</sup>				
Proximity to hospital				
Less than 100 km	1976 (33)	2278 (28)	929 (25)	
More than 100 km	556 (31)	713 (29)	270 (26)	
Median household income <sup>§</sup>				
Greater than \$32,000	1995 (33)	2106 (28)	723 (25)	
Less than \$32,000	537 (32)	885 (29)	476 (25)	
Proportion without high school <sup>§</sup>				
Less than 50%	1971 (33)	2128 (27)	826 (25)	
Greater than 50%	561 (33)	863 (29)	373 (26)	
Year of breast cancer diagnosis				
1992	348 (36)	514 (31)	288 (29)	
1993	371 (34)	489 (29)	218 (26)	
1994	420 (35)	515 (29)	198 (25)	
1995	453 (34)	494 (27)	194 (25)	
1996	431 (29)	520 (29)	156 (22)	
1997	509 (31)	459 (24)	145 (22)	

Table 5.3. Proportion of late-stage disease by selected characteristics and age

\*Charlson comorbidity index calculated one year prior to the diagnosis of breast cancer <sup>193</sup>.

<sup>=</sup> Diagnosed with a benign breast disease within 3 years before the diagnosis of breast cancer.

History of BBD	Age (years)	With prior mammogram	No prior mammogram	Crude Odds Ratio (95% CI*)	Adjusted Odds Ratio** (95% CI)
		% Late stage (No. of women late / early)	% Late stage (No. of women late / early)		
No	20-49	24 (136/440)	34 (2065/3939)	0.59 (0.48, 0.72)	0.62 (0.49, 0.76)
	50-69	21 (256/993)	30 (2465/5846)	0.61 (0.52, 0.71)	0.61 (0.53, 0.71)
	≥70	13 (30/197)	26 (1090/3111)	0.43 (0.29, 0.64)	0.42 (0.28, 0.62)
Yes	20-49	26 (124/351)	31 (207/457)	0.78 (0.60, 1.01)	0.80 (0.61, 1.07)
	50-69	19 (104/444)	27 (166/454)	0.64 (0.49, 0.85)	0.63 (0.48, 0.84)
	≥70	17 (18/88)	26 (61/174)	0.58 (0.33, 1.04)	0.60 (0.33, 1.11)

Table 5.4. Association between having a mammogram in 30 months before an episode of care and stage of disease, according to history of benign breast disease (BBD) and age

\*Cl, confidence interval

\*\*Adjusted for age, comorbidity, year of treatment.



Figure 5.1. Association between prior mammography and stage according to age

## Chapter 6. Overall Discussion and Conclusion

## Discussion

This is a health service study of breast cancer care, which includes investigations of variation of the patterns of care, determinants of waiting time, and the utilization of mammography before developing breast cancer. Waiting time was measured as the interval from the initial diagnostic procedure to the first surgery in a 6-year cohort (1992-1997) of 13,383 women with newly diagnosed primary breast cancer. The study used physician claims to a universal health insurance agency and hospitalization information from the province, thereby, providing an unbiased and reliable estimate of health services utilization and waiting time between procedures.

In order to understand the conceptual framework for the factors potentially associated with waiting time from the first procedure to the surgery, the determinants of pattern of care were studied. Pattern of care for breast cancer was measured as: the type of diagnostic procedures women received before surgery; the number of procedures received before surgery; and the type of surgery selected. Most women (78%) had a bilateral mammogram as their first procedure. Among women who started their episode of care with a biopsy (11%), 46% went on to have a less invasive procedure, such as a bilateral or unilateral mammogram. This may be the result of some women seeking a second opinion or could suggest that the biopsy was used prematurely in the diagnostic cycle.

Overall, 80% of women received breast conservative surgery (BCS). Similar to findings of other Canadian studies <sup>157,181</sup>, there was significant variation in the use of BCS across hospitals. This variation was only partly explained by the studied variables of the characteristics of women, surgeons and hospitals.

Over the period of this study, the number of diagnostic procedures received prior to surgery increased by almost 50%. One explanation for this finding could be that with increasing emphasis on screening, more questionable tumours are being identified <sup>183</sup> and the diagnostic process could be more difficult for these persons. Waiting time for breast cancer surgery also increased over this period in Quebec perhaps as the consequence of the increase in the numbers of procedures. Whether all procedures are needed is not known and is worthy of investigation. If the number of procedures used continues to increase at the present rate, the health care system may become overloaded. There was significant variation across hospitals for the probability of receiving three or more procedures (variance = 0.566, se = 0.103). Surgeon's age and number of surgeries performed per year explained 21% of hospital variation while hospital factors explained an additional 11% of variation across hospitals.

The overall median waiting time was 32 days with an interquartile range of 18 to 59 days. No statistically significant variation of waiting time was found across hospitals. Waiting time was determined by women's age, comorbidity, history of benign breast disease, distance to hospital, education level, type of surgery and

year when surgery was performed. Surgeon's age and the school of medical training, as well as hospital teaching status were also associated with waiting time. Waiting time for breast cancer surgery significantly increased during the last two years of this study: compared to 1992, adjusted waiting time in 1996 had increased by 14%, and in 1997 by 25%. Reductions in transfer payments from the federal government to the provinces occurred at this time and provincial governments reacted by closing hospitals, reducing health care budgets, and cutting hospital beds<sup>183,231</sup>. Other possible reasons for this increase may be the increased incidence of breast cancer and increased use of more diagnostic procedures before surgery.

Only 13.7% of women with breast cancer had had mammography during 30 months before their episode of breast cancer care. The benefit of prior mammography was similar to that represented by in the clinical trials<sup>211,212,220</sup> which indicated a 39% reduction in late-stage breast cancer among women between 50 an 69 years of age, and a 58% reduction in women aged 70 years and older. These findings are in agreement with data from randomized screening trials, thereby, confirming the importance of organized population-based screening programs.

The modelling strategy had an important influence on the results of the associations between predictors and waiting time, or pattern of care at the hospital and physician levels. Comparing hierarchical models with conventional regression

models showed that with the hierarchical models the standard errors of the regression coefficients increased, indicating that intra-cluster correlation needs to be taken into account. Hierarchical modelling strategies are, therefore, warranted. Conventional logistic regression ignores clustering and generally causes the standard errors of regression coefficients to be underestimated, thus inflating the statistical significance of the effects. For variables measured at the individual level (women's characteristics) the estimates of effect and variation derived from the hierarchical logistic model did not differ from those derived from conventional logistic regression. Estimates of effect for hospital and surgeon factors were also similar using hierarchical logistic models, but the standard errors were much larger than were those from the conventional models, rendering these terms statistically non-significant. When analyzed with conventional logistic regression, physician's school of graduation and surgical volume, and hospital caseload and teaching status were all significantly associated with pattern of care (Appendix 3: table A3.2). However, after using hierarchical modelling, these effects lost their statistical significant. Similarly, with conventional linear regression, the annual number of breast surgeries performed by each surgeon and the annual number of discharges for breast disease at each hospital were significantly associated with waiting time (Appendix 3: table A3.1), but lost their statistical significance when included in the hierarchical model.

The results of this study should be interpreted in light of several known strengths and weakness of the data sources. Physician claims data, while not designed for

research purpose, lend themselves well to certain areas of health care service research. This data source provides an accurate reflect of the number, type, and timing of clinical procedures and activities, and permits identification several key variables related to health care services. Hospital discharge data provides a primary diagnosis and 15 secondary diagnosis for the hospitalization or day-surgery, as well as invasive procedures performed during hospitalization or day-surgery. Linkage of the two databases provided us with accurate data regarding clinical procedures and clinical diagnosis, which are the key pieces of information needed to answer the specific questions. Both databases provided an efficient alternative to studies of medical charts or encounter records.

The important limitation of these databases is that they do not include any information to separate the components of patient delay from provider delay. Some information that may be potentially important for determining waiting time was not available from the administrative database. We were only able to measure a few of the variables in the conceptual model. We were not able to determine, for example, whether or not a woman had a family history of breast cancer, a factor with potential to influence both woman and physician's decision-making. Nor were we able to measure women's genetic profile, health care behaviour and other psychosocial factors, practice organisation and infrastructure. That may be the reason that over 60% of total variation of waiting time remained unexplained. The fact that over half of the variation of waiting time could not be explained by the

information available in the databases indicate that a better understanding of the mechanism for delay will require more direct sources of information.

A further limitation of the data is that no differentiation is made between screening and diagnostic mammograms on the physician's claims. In Quebec, the claim's code identifies mammograms only by procedure (bilateral, unilateral or needlelocalization) not by clinical indication (screening or diagnostic). Assuming all bilateral mammograms were for screening purpose would introduce serious bias into estimations of screening mammography utilisation<sup>224</sup>. For this reason, we created the concept of episode of care and tried to examine the prior mammography separately among women with and without a history of benign breast disease. This provided us with a more distinct group to infer prior mammography for screening purpose.

## Implications

This work has positive implications for the use of administrative databases in health services research. Medical service databases offer an attractive alternative to patient and hospital surveys for monitoring the waiting time for treatment of other diseases as well as the utilization of health care services by the population. Administrative data does not provide information on whether factors such as physician recommendation and/or patient behaviours and preferences affect the uptake of certain diagnostic or treatment procedures, or waiting time. For this reason, national and provincial surveys continue to serve as the main data

sources for research impacting on health policy. As mentioned in the review of the literature<sup>37,104,180</sup>, however, one of the persistent problems with previous studies of delay and the factors associated with delay in cancer treatment is small sample sizes, which produce unreliable delay rates and diminished power to detect the associations. Research based on administrative data has the advantage of large sample sizes, thus providing an efficient way of monitoring waiting time and of examining broader issues such as patterns of care and the factors affecting breast cancer treatment.

This study has also developed methodological features that may be applied by researchers using administrative data for the investigation of waiting time for treatment of other cancers. For example, this study provides the methods for defining the stage of disease using administrative data. This is useful for researchers who have no detailed medical information available to them except what is contained in the administrative database. Moreover, this study demonstrated the application of hierarchical models for the evaluation of multi-level data structure in health care service research. Hierarchical modelling allows us to study the effects of characteristics at three levels (e.g., level of the patient, physician and hospital) simultaneously after taking into account the cluster effect, and to partition variations of the study outcome from each level.

The implications of the study results for health policy indicate the need for a global solution. The lack of a statistically significant variation of waiting time across

hospitals and surgeons implies that the observed waiting times, which might be considered long, are not concentrated in only a few hospitals or surgeons, but widespread. Therefore, to reduce overall waiting time, strategies would need to be systematically applied. Possible solutions are increasing the co-ordination of care so that all breast cancer services are offered in one setting and overseen in a consistent manner. In such a setting, unexpectedly long delays could be flagged for intervention so that unnecessarily long waiting times may be prevented.

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