# Elapsed time from breast cancer detection to first adjuvant therapy in a Canadian province, 1999–2000

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Abstract

**Background:** A number of studies have examined time intervals between care steps in breast cancer diagnosis and treatment. The objective of this study was to document the elapsed time from first clinical or mammographic detection of breast abnormality to initiation of first adjuvant therapy in women with invasive breast cancer in Nova Scotia and to examine the effect of age, disease stage and place of residence on these intervals.

**Methods:** All dates were abstracted from patient charts and the Oncology Patient Information System. Eligible women were those with invasive breast cancer detected by Sept. 1, 1999, who were referred to 1 of 2 provincial cancer treatment centres by Sept. 1, 2000. All time intervals were calculated in days, and only patients experiencing both care events defining an interval were included in the analysis of time to event for that interval. We used proportional hazards regression analysis to evaluate the influence of patient age, disease stage and place of residence on times between care events.

**Results:** A total of 776 new diagnoses of breast cancer were reported to the Nova Scotia Cancer Registry over the study period. Of the 776, 467 met the inclusion criteria, and 364 patients were eligible for analysis. The overall median time from clinical or mammographic detection of breast cancer to initiation of first adjuvant therapy was 91 days (interquartile range 72–123 days). Disease stage was the strongest predictor of elapsed time: the median interval from disease detection to initiation of first adjuvant therapy for patients with stage I disease was 118 days, as compared with 85 days for those with stage II disease and 75 days for those with stage III disease (adjusted hazard ratio [HR] 2.1, 95% confidence interval [CI] 1.6–2.8). Patients aged 70 years or more at diagnosis experienced longer elapsed times (median interval 98 days) than did younger patients (93 days for those aged 50–69 years and 82 days for those aged 49 years or less) (adjusted HR 1.6, 95% CI 1.1–2.4).

**Interpretation:** Women aged 70 or more and those with stage I breast cancer experienced longer elapsed times from disease detection to initiation of first adjuvant therapy than did younger women and those with more advanced disease. These findings may have implications for the design of interventions to minimize intervals between steps in breast cancer care and should be validated within the Canadian context. Future investigation exploring the full spectrum of breast cancer care may lead to a more complete understanding of processes and gaps in the current system.

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Time intervals for isolated care steps in the diagnosis and management of breast cancer have been evaluated in a number of publications from Canada, Germany and the United Kingdom. These studies have focused on time to first surgical intervention,[1] time to pathological confirmation of invasive disease[2] or a composite interval spanning onset of symptoms to initiation of first treatment, which, in the vast majority of cases, is surgical intervention.[3–6] The spectrum of care for potentially curable breast cancer, however, extends from initial detection to completion of all adjuvant therapies and has become increasingly complex and multidisciplinary. Patients interact with a sequence of various health care professionals and undergo a series of procedures at various medical facilities or in different areas of a large hospital. Most patients are referred for 1 or more adjuvant therapies (radiation, chemotherapy or hormonal therapy), all of which have been shown to reduce the risk of locally recurrent or metastatic disease and to improve overall survival in appropriately selected patients.[7–9] Although the time from referral to initiation of adjuvant therapy is a critical component in breast cancer care, it has not been included in previous analyses of elapsed times in breast cancer care.

The first objective of our study was to document elapsed times from date of mammographic or clinical detection of breast abnormality to initiation of first adjuvant therapy for women with invasive breast cancer. Our second objective was to examine the influence of age, disease stage and place of residence at the time of diagnosis on this elapsed time.

## Methods

There are 2 comprehensive cancer centres in Nova Scotia, 1 in Halifax and the other in Sydney. The cancer centre treatment database maintains a complete record of information for all patients referred to the centres. Original dated copies of all mammographic, diagnostic, surgical and pathological reports are included in each patient chart. Patient records capture the date of initial written referral, the date of receipt of the referral at the centre and the date of patient contact following receipt of the referral. The dates of all appointments with medical and radiation oncologists as well as dates of chemotherapy and radiotherapy administration are also recorded. The Oncology Patient Information System is a computerized register of all cancer diagnoses and deaths in Nova Scotia since 1964 and is composed of the Nova Scotia Cancer Registry and the provincial cancer centre treatment databases.

All female patients with a new diagnosis of invasive breast

carcinoma who were referred to 1 of the 2 comprehensive cancer centres in Nova Scotia were eligible for the study. For inclusion, patients had to have had their initial breast abnormality detected by Sept. 1, 1999, and to have been referred to 1 of the 2 provincial cancer centres by Sept. 1, 2000. Patients with in-situ disease (ductal or lobular) were excluded, as were those with newly diagnosed metastatic disease. All other cases were eligible for analysis.

Dates of diagnosis and surgery were abstracted by 2 of us (D.C. and D.R.) from original radiologic, surgical and pathological reports. All other dates were abstracted from the cancer centre chart or the Oncology Patient Information System, or both. In cases of discrepancy, we used dates from the cancer centre chart, as this contained all original-source documentation and is the most complete source of information for all referred patients. The only event that was captured but did not have a clearly documented date was clinical detection of breast cancer. For these cases, we approximated the date by reviewing clinic notes or the original referral letter, or both. If the date of detection remained unclear, we used the date of the first abnormal radiographic evaluation (mammography or ultrasonography). The only missing values were those for an event not experienced by an individual patient.

Time intervals abstracted included (1) date of first abnormal mammogram or clinical detection of breast abnormality to pathological confirmation of invasive disease; (2) pathological confirmation of invasive disease to date of final definitive surgery (defined as modified radical mastectomy, lumpectomy with pathologically clear margins, re-excision for positive margins after lumpectomy or axillary dissection following lumpectomy, if done on separate dates); (3) date of final definitive surgery to receipt of referral at the cancer centre; (4) receipt of referral to date of patient contact by the cancer centre referral office; (5) date of patient contact to date of first appointment with a medical or radiation oncologist; and (6) date of first appointment to date of initiation of first adjuvant therapy. All intervals were calculated in days, and only the data for subjects who experienced both events defining an interval were included in the analysis of that interval.

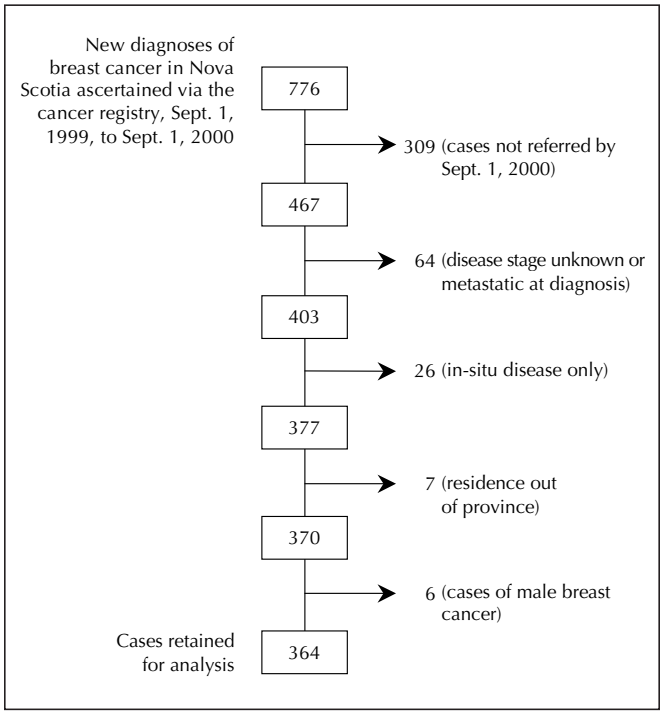


**Fig. 1: Subjects available for analysis and reasons for exclusion.**

We used proportional hazards regression analysis to evaluate the influence of each of the 3 patient characteristics (age, disease stage and place of residence) on the time intervals. Covariates were parameterized such that hazard ratios (HRs) greater than 1 are associated with patients whose intervals are longer than those of patients in the reference category. We tested the validity of the proportional hazards assumption informally by visual examination of the plots of the log-log transformed hazard function, stratified by levels of the covariate.

For each time interval examined, we fit proportional hazards models with each covariate univariately and for a final model with all 3 covariates fit simultaneously. We used Wald-type significance tests to test the hypothesis that the estimated covariate parameters were null.

## Results

A total of 776 new diagnoses of breast cancer were reported to the Nova Scotia Cancer Registry over the study period. Of the 776, 467 met the inclusion criteria, and 364 patients were eligible for analysis. Eligible patients and reasons for exclusion are presented in Fig. 1. The place of residence, age and disease stage of the 364 patients are presented in Table 1. The median age was 57 (range 25–87) years.

The median time (and interquartile range) for each of the 6 intervals assessed are shown in Table 2. Overall, the median time from disease detection to start of first adjuvant therapy was 91 days, with 75% of the patients starting adjuvant therapy within 123 days after disease detection.

Table 3 shows the median times (and interquartile ranges) for selected care steps according to the covariates of age, disease stage and place of residence. The multivariate analysis of intervals according to the 3 covariates is presented in Table 4. Compared with younger patients, those

**Table 1: Characteristics of women with a new diagnosis of invasive breast cancer referred to Nova Scotia cancer centres between Sept. 1, 1999, and Sept. 1, 2000**

| Characteristic | No. (and %) of patients |
|---|---|
| **Place of residence** | |
| Cape Breton Island | 54 (14.8) |
| Halifax and Hants counties | 175 (48.1) |
| Elsewhere in province | 135 (37.1) |
| **Age, yr** | |
| ≤ 49 | 102 (28.0) |
| 50–69 | 181 (49.7) |
| ≥ 70 | 81 (22.2) |
| **Disease stage** | |
| I | 155 (42.6) |
| II | 198 (54.4) |
| III | 11 (3.0) |

aged 70 years or more experienced a significantly longer interval from receipt of referral at the cancer centre to initiation of first adjuvant therapy (adjusted HR 2.0, 95% confidence interval [CI] 1.4–2.8, $p < 0.01$). Older patients also experienced a significantly longer interval from disease detection to initiation of first adjuvant therapy (adjusted HR 1.6, 95% CI 1.1–2.4, $p < 0.05$). Patients with stage I disease experienced a significantly longer interval from disease detection to initiation of first adjuvant therapy than did patients with stage II or III disease (adjusted HR 2.1, 95% CI 1.6–2.8, $p < 0.01$). The intervals from disease detection to receipt of referral (adjusted HR 1.7, 95% CI 1.3–2.2, $p < 0.01$) and from receipt of referral to initiation of first adjuvant therapy (adjusted HR 1.3, 95% CI 1.0–1.7, $p < 0.05$) were also significantly longer for patients with stage I disease. Place of residence had a minimal effect on time intervals; however, patients residing on Cape Breton Island experienced a significantly shorter interval from receipt of referral to initiation of adjuvant therapy than did those living elsewhere in the province (adjusted HR 0.7, 95% CI 0.5–1.0, $p < 0.05$).

In most specialized outpatient care facilities in Canada, initiation of consultative and other procedures depends on receipt of a written referral from a physician. In total, a median of 31 days (interquartile range 23–42 days) elapsed from date of definitive surgery to first contact of the patient by the cancer centre. A median of 11 days elapsed from first oncologic appointment to initiation of first adjuvant therapy. This overall median interval, however, does not take into account different types of adjuvant therapy received. The median time from first oncologic appointment to start of first adjuvant therapy was 7 days for chemotherapy and 36 days for radiation therapy. For hormonal therapy, a simple prescription is required, and no specific date is entered in the patient chart. The median interval, therefore, was assumed to be 0 days.

## Interpretation

Our data document a median elapsed time of 91 days from initial detection of breast cancer to start of first adjuvant therapy, with 25% of patients experiencing a median interval of greater than 123 days. Patients with stage I disease experienced longer intervals than did those with more advanced disease, and patients aged 70 years or more experienced longer intervals than younger patients. A median of 31 days elapsed from date of definitive surgery to first contact of the patient by the cancer centre.

Previous studies from Canada, the United Kingdom and Germany have focused on time intervals from breast cancer detection to first surgical intervention.[1–6] The full spectrum of breast cancer care, however, extends from diagnosis to completion of all adjuvant therapies. Our data are not directly comparable to data from previous studies, as the care intervals and patient inclusion criteria differ. As well, extending the analysis to start of first adjuvant therapy expands the number of care intervals assessed and will obviously lead to a longer overall median care timeline.

There are few data on the optimal timing of sequential steps in breast cancer care. The Canadian Breast Cancer Screening Initiative recommends that the interval from initial screening examination to any diagnosis for 90% of patients should be 5 weeks, or 7 weeks if an open biopsy procedure is required.[10] The median interval in our cohort was 13 days (interquartile range 7–28 days). Our data, however, are restricted to women with pathologically confirmed invasive cancer, many of whom did not receive their diagnosis through a screening program and some of whom did not undergo initial mammographic evaluation. Thus, this finding is not directly comparable to data from breast screening programs. The Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer recommends that local breast irradiation should commence

**Table 2: Median time for the 6 care intervals assessed**

| Interval | Detailed events | | No. of patients* | Median time† (and interquartile range), d |
|---|---|---|---|---|
| | From | To | | |
| Disease detection to cancer centre referral | Detection‡ | Biopsy | 245 | 13 (7–28) |
| | Biopsy | Surgery | 173 | 19 (13–26) |
| | Surgery | Receipt of referral | 192 | 16 (10–23) |
| Summary | Detection | Receipt of referral | 260 | 56 (41–77) |
| Referral receipt to start of first adjuvant treatment | Receipt of referral | First contact | 356 | 11 (4–20) |
| | First contact | First appointment | 337 | 6 (0–13) |
| | First appointment | First adjuvant therapy | 290 | 11 (4–29) |
| Summary | Receipt of referral | First adjuvant therapy | 296 | 36 (27–48) |
| Overall | Detection | First adjuvant therapy | 223 | 91 (72–123) |

*Only patients who experienced both events defining the interval were included.
†Time by which 50% of patients have experienced end point.
‡Includes patients whose disease was initially detected clinically or mammographically.

within 12 weeks after surgery if not preceded by chemotherapy[11] and that adjuvant chemotherapy begin as soon as possible after surgical healing.[12] In most of the randomized trials documenting a benefit for adjuvant chemotherapy, therapy was started within 4 to 10 weeks of surgery.[13–15]

The time intervals noted above provide a framework for evaluating specific elements of care for a patient with newly diagnosed disease. However, comprehensive breast cancer care involves an interrelated series of evaluation and therapy steps, all of which pose threats to emotional, psychological and, perhaps, physical well-being.[4,5,16,17] Regional cancer centres were developed to address the specialized needs of patients with cancer and the multidisciplinary nature of their care. Unfortunately, most cancer care is still delivered in sequential fragments. A truly multidisciplinary approach would incorporate a simultaneous rather than a sequential decision

**Table 3: Distribution of covariates examined and median times to selected care events**

| | Care interval | | | | | |
|---|---|---|---|---|---|---|
| | Disease detection to receipt of referral | | Receipt of referral to first adjuvant therapy | | Disease detection to first adjuvant therapy | |
| Covariate | No. of patients* | Median time (and interquartile range), d | No. of patients* | Median time (and interquartile range), d | No. of patients* | Median time (and interquartile range), d |
| **Area of residence** | | | | | | |
| Cape Breton Island | 36 | 61 (45–74) | 45 | 30 (19–42) | 33 | 89 (64–117) |
| Halifax and Hants counties | 131 | 57 (41–82) | 143 | 37 (29–49) | 116 | 95 (79–126) |
| Elsewhere in province | 93 | 54 (36–71) | 108 | 36 (26–49) | 74 | 86 (71–123) |
| **Age, yr** | | | | | | |
| ≤ 49 | 71 | 52 (40–74) | 91 | 32 (23–42) | 63 | 82 (70–112) |
| 50–69 | 137 | 57 (42–77) | 151 | 37 (27–48) | 119 | 93 (73–125) |
| ≥ 70 | 52 | 58 (39–82) | 54 | 43 (29–57) | 41 | 98 (80–140) |
| **Disease stage** | | | | | | |
| I | 114 | 64 (48–97) | 115 | 41 (30–54) | 88 | 118 (85–141) |
| II | 141 | 51 (35–68) | 171 | 34 (25–46) | 130 | 85 (70–99) |
| III | 5 | 36 (36–57) | 10 | 34 (18–41) | 5 | 75 (70–89) |
| All subjects | 260 | 56 (41–77) | 296 | 36 (27–48) | 223 | 91 (72–123) |

*Only patients who experienced both events defining the interval were included.

**Table 4: Multivariate analysis of time to care events**

| | Care interval | | | | | |
|---|---|---|---|---|---|---|
| | Disease detection to receipt of referral | | Receipt of referral to first adjuvant therapy | | Disease detection to first adjuvant therapy | |
| Covariate | Univariate HR† | Adjusted HR (and 95% CI)‡ | Univariate HR† | Adjusted HR (and 95% CI)‡ | Univariate HR† | Adjusted HR (and 95% C1)‡ |
| **Place of residence** | | | | | | |
| Cape Breton Island | 1.0 | 1.2 (0.8–1.7) | 0.7 | 0.7 (0.5–1.0)§ | 0.7 | 0.8 (0.5–1.1) |
| Halifax and Hants counties | 1 | 1 (reference) | 1 | 1 | 1 | 1 |
| Elsewhere in province | 0.9 | 0.9 (0.7–1.2) | 1.0 | 0.9 (0.7–1.2) | 0.9 | 0.9 (0.7–1.2) |
| **Age, yr** | | | | | | |
| ≤ 49 | 1 | 1 (reference) | 1 | 1 | 1 | 1 |
| 50–69 | 1.3 | 1.1 (0.8–1.5) | 1.3 | 1.3 (1.0–1.6) | 1.4 | 1.2 (0.8–1.6) |
| ≥ 70 | 1.4 | 1.4 (1.0–2.0) | 1.8 | 2.0 (1.4–2.8)¶ | 1.5 | 1.6 (1.1–2.4)§ |
| **Disease stage** | | | | | | |
| I | 1.6 | 1.7 (1.3–2.2)¶ | 1.3 | 1.3 (1.0–1.7)§ | 2.0 | 2.1 (1.6–2.8)¶ |
| II | 1 | 1 (reference) | 1 | 1 | 1 | 1 |
| III | 0.7 | 0.6 (0.3–1.5) | 0.7 | 0.7 (0.3–1.2) | 0.7 | 0.7 (0.3–1.7) |

Note: HR = hazard ratio, CI = confidence interval.
*From proportional hazards regression models.
†Not accounting for other covariates. This column represents the results of 3 separate univariate models.
‡Adjusted for remaining covariates. This column represents the results of a single multivariate model.
§$p < 0.05$ (Wald test).
¶$p < 0.01$ (Wald test).

and treatment process. Although the patient needs time between each step of care to digest information and recover from procedures, intervals of weeks may heighten anxiety, frustration and potential mistrust of the cancer care system.

There are a number of limitations to our study. Since we analyzed only referred cases, our data do not provide a population-based description of breast cancer care timelines. Patients who were never referred to the centres, were referred after Sept. 1, 2000, or who received their oncologic care elsewhere were excluded. Therefore, the data do not capture the entire patient population who might otherwise meet the eligibility criteria. A 1-year timeframe is relatively short and does not allow for the evaluation of trends in care, and it may be subject to acute changes in resources affecting components of care. However, no significant health care reorganization issues were observed during the study period. We deliberately excluded referrals for in-situ and metastatic disease, and thus our data are not applicable to these groups. We did not assess important variables that may have affected each time interval, including number and types of radiographic and surgical procedures, differences in clinical presentation and time taken to complete staging evaluations, when performed. Treatment variables that may have influenced intervals, such as delayed wound healing, surgical complications and coexisting disease, were not captured. Finally, we were unable to assess important patient variables, such as distance to treatment centre, as well as patient-initiated treatment and appointment delays. Time to initiation of first adjuvant therapy was the last interval analyzed. Therefore, the experience of women who received a number of adjuvant therapies (i.e., chemotherapy followed by radiation therapy) was incompletely assessed.

Although most of the women in our cohort received breast cancer care within generally accepted timeframes, for many patients and providers a median elapsed time of 91 days from disease detection to start of first adjuvant therapy may seem unacceptably long. As well, 25% of those in our cohort experienced an overall elapsed time of greater than 123 days. The finding of a significant influence of older age (70 years or more) at diagnosis and earlier stage disease on the overall elapsed time suggests possible target patient populations for interventions aimed at reducing time intervals. A median interval of 16 days from date of definitive surgery to receipt of referral at the cancer centre and a further 36 days from referral receipt to initiation of first adjuvant therapy suggest a potential target for improvements in multidisciplinary communication and for development of support and information programs for patients as they wait. These results should be validated within the Canadian context, with future investigations exploring the full spectrum of care to more fully elucidate reasons for delay and to achieve a more complete understanding of time intervals in breast cancer care.

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