Breast cancer survival by teaching status of the initial treating hospital

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Abstract

Background: A number of studies have documented variation in treatment patterns by treatment setting or by region. In order to better understand how treatment setting might affect survival, we compared the survival outcomes of women with node-negative breast cancer who were initially treated at teaching hospitals with those of women initially treated at community hospitals.

Methods: We constructed a retrospective cohort consisting of a random sample of 938 cases, initially diagnosed in 1991, drawn from the Ontario Cancer Registry. Exposure was defined by the type of hospital in which the initial breast cancer surgery was performed. Outcomes were ascertained through follow-up of vital statistics.

Results: The crude 5-year survival rate was 88.7% for women who had their initial surgery in a community hospital and 92.5% for women who had their initial surgery in a teaching hospital. Women in higher income neighbourhoods experienced better survival at 5 years regardless of which type of hospital they were treated in. Multivariate proportional hazards regression modelling demonstrated a 53% relative reduction in risk of death among women with tumours less than or equal to 20 mm in diameter who were treated at a teaching hospital (relative risk [RR] = 0.47, 95% confidence interval [CI] 0.23–0.96), whereas among those with larger tumours there was no demonstrated difference in survival (RR = 1.32, 95% CI 0.73–2.32). Other variables that were significant in the model were age at diagnosis, estrogen receptor status and the use of radiation therapy.

Interpretation: Women with node-negative breast cancer and tumours less than or equal to 20 mm in diameter who were initially seen at a teaching hospital had significantly better survival than women with similar tumours who were initially seen at a community hospital. Survival among women with larger tumours was not statistically significantly different for the 2 types of hospital.

Many studies have demonstrated variation in treatment for breast cancer across regions and populations. These variations include different patterns of initial breast surgery,[1,2] use of chemotherapy,[3] hormone therapy[4] and radiation therapy.[5,6] Characteristics of both patients and care providers have been related to these variations. One key factor that has been considered is the teaching or academic status of both the treating physician and the institution where care is provided. A major point of contention is whether these variations are related to differences in outcomes.

Variations in care may lead to different outcomes through different access to services or different use of proven therapies. Certain physicians may acquire greater skills through frequently dealing with certain types of case, as has been suggested in studies of the volume–outcome relationship.[7] Teaching status may affect patient outcomes directly because of better knowledge and skills or indirectly as a result of improved processes of care, such as the use of multidisciplinary clinics. Breast cancer survival has been shown to vary by region and socio-economic status,[8–10] as well as by hospital and physician characteristics.[11–16]

We located 6 published studies examining the relationship between hospital or surgeon characteristics and breast cancer survival. Of these, 4 considered hospital size or teaching status[11–13,16] and 2 considered surgeon specialization.[14,15] Five of the 6 studies demonstrate better survival where initial surgery was performed at large or specialized centres. All but one of these studies[15] have been synthesized in a review

Research

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by Grilli and colleagues,[17] who report a significant pooled odds ratio of 0.82 (95% confidence interval [CI] 0.77–0.88), showing a reduction in risk of death. The cohorts for these studies were constructed over a period of 6–11 years prior to 1990. Treatment information was available for only 3 of the 6 studies, and not all were able to control for stage of disease.

This study compares the 5-year survival of women with node-negative breast cancer who received initial surgical treatment in teaching hospitals with those treated in nonteaching hospitals, while controlling for potential confounders. Because the cohort we examined is composed of women diagnosed in the same year with well-defined localized cancer, variation in stage is unlikely to play a role in our findings.

Methods

We conducted a retrospective, population-based, cohort study by identifying cases of node-negative breast cancer that were newly diagnosed in 1991 in Ontario. This study is based on an earlier study that compared patterns of practice for breast cancer in 2 Canadian provinces.[2] The Ontario Cancer Registry, which has been shown to have a high level of coverage,[18,19] was used to select cases. Because the cancer registry does not contain detailed information on cancer stage, the records of all cases that met the basic inclusion criteria were further reviewed to assess eligibility for the study.

The basic inclusion criterion was that nodal status was confirmed to be negative by pathologic examination. Patients for whom management was more likely to be complex or who were less likely to receive standard treatments were excluded. Patients thus excluded were those over 90 years of age, those whose breast cancer was diagnosed by death certificate only or who died within 30 days of diagnosis, those with nonepithelial forms of cancer, those with previous invasive cancer or breast carcinoma in situ, those with tumours extending to the chest wall or skin, and those with bilateral breast cancer or carcinoma in situ. Cases in which initial treatment was provided out of province were also excluded. In addition, cases from one community hospital and one cancer center were excluded because the institutions did not participate in our study. The baseline characteristics of these cases were not different from those of the whole sample. Construction of the cohort, physician characteristics and the proportion of cases excluded are described in detail elsewhere.[2]

Data elements required for the study were identified and defined before data were collected. On the basis of the framework proposed by Deber and Thompson,[20] the data were grouped into categories by patients' demographic variables (age and region of residence), tumour characteristics (size, margins, location, and lymphatic, vascular or neural invasion, and extent of ductal carcinoma in situ), physician characteristics (year of graduation from medical school and academic affiliation), hospital characteristics (teaching status and number of beds) and treatments received (type of surgery and use of radiation and systemic therapy). All information held in the cancer registry in electronic form was retrieved first, followed by centrally stored paper documents (e.g., reports from pathologic examinations) and by information from other databases (e.g., drug data and physician billings). Next, data abstractors reviewed information contained in medical records at cancer centres and larger hospitals. Finally, the remaining information was sought by writing to hospital records departments or to the physician most involved in a particular patient's care.

Hospital teaching status was assigned according to the 1991 Canadian Hospital Directory,[21] which defines teaching hospitals as those with membership in the Association of Canadian Teaching Hospitals. Information about physician characteristics was obtained through the 1991 Canadian Medical Directory and about hospital characteristics from the 1991 Canadian Hospital Directory.[21] Before this information was merged with other data, names and other identifying information were removed. The patients' socio-economic status was inferred from the "forward sortation area" of each patient's postal code.[22] Each forward sortation area includes a population of approximately 10 000; the median family income for each area was obtained from the 1991 census. For analysis, the median incomes were divided into 2 equal groups, based on statistical power considerations.

The data abstractors were certified health records technicians who were trained as a group at the start of the study. There were regular quality control checks including duplicate reviews. Any discrepancies or items of concern with which the abstractors had difficulty were reviewed in conjunction with the investigators. Throughout the study, the anonymity of patients, physicians and hospitals was preserved. The study was approved by all relevant institutional ethics committees.

For each case, the most definitive surgical procedure performed within 6 months of diagnosis was assessed. On the basis of a review of reports from pathologic examinations and of notes from surgery, the abstractor categorized each procedure as a mastectomy or as breast-conserving surgery (BCS), which included any procedure less extensive than a mastectomy. Radiation therapy for the initial treatment was defined as a course of radiation treatment begun within 12 months of diagnosis that was not for a recurrence of cancer.

The main outcome, survival after breast cancer, was assessed by linking the cohort back to the Ontario Cancer Registry.[23] The registry receives copies of mortality data based on death registrations from the Ontario Registrar General. In addition, the registry links data about death notifications from cancer centres and in-hospital deaths of patients who had a cancer diagnosis. The current analysis was based on mortality records through to Dec. 31, 1996. Cause of death was assessed and coded using the International Classification of Diseases, ninth revision,[24] based on information on the death certificate. The death certificates were reviewed for all subjects in the cohort known to have died in order to ascertain the recorded principal and contributing causes of death and to verify the primary cause.

Descriptive statistics were used to compare the case mix of women initially treated at teaching hospitals versus community hospitals. Kaplan-Meier survival curves and the Cox proportional hazards model were used to assess the relationship between individual explanatory variables and survival outcomes. A multivariate proportional hazards regression model was developed, initially grouping variables by patient, tumour, treatment and provider characteristics. Interactions between each of the significant variables and the main exposure, teaching status, were assessed. Survival time was calculated as the time between date of diagnosis and date of death.

Results

The final cohort was composed of 938 women diag-

nosed with breast cancer in 1991. Of these women, 292 (31%) had had their initial surgery at a teaching hospital. Table 1 summarizes the characteristics of these women by initial treating hospital. The 2 populations were similar with respect to distribution by socio-economic status (median neighbourhood family income) and proportion living in urban residences. Neighbourhood income was divided based on the median value; however, using other cutoff points did not change the results. Distance to the nearest radiation treatment facility, which was also used as means of considering issues of accessibility, did not provide additional information.

Table 1: Distribution of characteristics by type of hospital where surgery was initially performed

Characteristic	No. (and %) of patients*		Odds ratio (and 95% CI)
	Community hospital	Teaching hospital	
No. of women	646	292	
No. (and %) of deaths (all causes)	85 (13)	26 (9)	
No. (and %) of deaths from breast cancer	55 (9)	15 (5)	
Mean age, yr	60	58	
Age, yr			
< 50	149 (23)	85 (29)	1.44 (1.01–2.06)
50–64	249 (39)	109 (37)	1.11 (0.80–1.53)
≥ 65	248 (38)	98 (34)	1.00
Family income < $ 45 000	337 (52)	159 (54)	1.10 (0.83–1.45)
Urban residence	542 (84)	258 (88)	1.46 (0.96–2.20)
Mean tumour size, mm	18.5	17.6	
Tumour size ≤ 20 mm	436 (67)	211 (72)	1.28 (0.94–1.75)
Tumour grade			
Well-differentiated	59 (9)	43 (15)	1.00
Moderate	169 (26)	139 (48)	1.13 (0.72–1.77)
Poor	129 (20)	57 (20)	0.61 (0.37–1.00)
Unknown	289 (45)	53 (18)	0.25 (0.15–0.41)
ER status			
Positive	409 (63)	188 (64)	1.00
Negative	137 (21)	44 (15)	0.70 (0.48–1.02)
Missing	100 (15)	60 (21)	1.31 (0.91–1.88)
Extensive DCIS	78 (12)	54 (18)	1.65 (1.13–2.41)
Multifocal tumour	40 (6)	33 (11)	1.93 (1.19–3.13)

Note: CI = confidence interval, ER = estrogen receptor, DCIS = ductal carcinoma in situ.
*Unless stated otherwise.

Women seen in teaching hospitals were significantly younger, had smaller tumours and were more likely to be diagnosed with multifocal disease and extensive ductal carcinoma in situ. Information about tumour grade was more likely to be missing for women seen in community hospitals. However, data about estrogen receptor status were missing more often for women seen at teaching hospitals, which is contrary to information reported in other studies.

The proportion of women receiving different modes of therapy is shown in Table 2. Women seen in teaching hospitals were significantly more likely to receive BCS and adjuvant therapy, and they had a greater number of lymph nodes examined. They were less likely to be treated with surgery alone.

The crude 5-year survival rate was 88.7% for women having initial surgery in a community hospital and 92.5% for women with initial surgery in a teaching hospital (p = 0.07). Women in higher income neighborhoods experienced better survival at 5 years whether they were treated at community or teaching hospitals (Table 3). Fig. 1 shows the 5-year Kaplan-Meier survival curves stratified by hospital type.

The results of proportional hazards regression modelling are presented in Table 4. Modelling the effect of hospital type on its own showed a 33% reduction in risk for women seen at teaching hospitals (relative risk [RR] = 0.67, 95% CI 0.53–1.03). In the multivariate model, a significant interaction was noted between size of tumour and the type of hospital at which initial surgery was performed. Women with tumours less than or equal to 20 mm in diameter experienced a 53% reduction in risk of death (RR = 0.47,

Table 2: Treatment received, by type of hospital where surgery was initially performed

Treatment	No. (and %) of patients*		Odds ratio (and 95% CI)
	Community hospital	Teaching hospital	
Breast-conserving surgery (BCS)	422 65)	212 (72)	1.41 (1.04–1.91)
Radiation therapy following BCS	306 (73)	173 (82)	1.67 (1.10–2.52)
Chemotherapy	50 (8)	20 (7)	0.88 (0.51–1.51)
Hormone therapy	196 (30)	67 (23)	0.67 (0.46–0.92)
Surgery only	198 (31)	72 (25)	0.72 (0.53–0.99)
Mean no. of nodes sampled	9.2	11.1	
≥ 10 nodes sampled	272 (42)	172 (59)	1.95 (1.47–2.59)

*Unless stated otherwise.

95% CI 0.23–0.96) if initial surgery was carried out in a teaching hospital, whereas no difference was found among those with larger tumours (RR = 1.32, 95% CI 0.73–2.32). The effect of hospital type on survival did not vary greatly with the introduction or removal of treatment variables.

The power for disease-specific analysis was quite limited (Table 1). Multivariate modelling of breast cancer deaths alone did not show any a significant difference in survival (RR = 0.74, 95% CI 0.41–1.32).

Interpretation

This study demonstrates a survival advantage for women with small tumours who underwent initial surgery at a teaching hospital. Although this advantage appears small in absolute terms, it is comparable to that observed for adjuvant systemic therapy. The difference is not explained by patient characteristics, such as age or socio-economic status, disease stage or treatment variables. Accounting for patient case mix increased the difference in survival.

Table 3: Crude 5-year survival estimates

	% of patients (and 95% CI)	
Stratification variable	Community hospital	Teaching hospital
Hospital type	88.7 (86.3–99.1)	92.5 (89.4–95.5)
Median neighbourhood family income, $		
< 45 000	87.8 (84.3–91.3)	89.9 (95.3–94.6)
≥ 45 000	89.6 (86.2–93.0)	95.4 (92.0–99.0)
Tumour size, mm		
≤ 20	90.6 (87.9–93.3)	95.7 (93.0–98.5)
> 20	84.3 (79.3–89.3)	83.1 (74.7–91.5)

There are several possible explanations for our results. First, there may be differences in the 2 patient populations in terms of characteristics not controlled for in the analysis. There may be different patterns of use of early detection and other diagnostic tests among women who seek treatment at different facilities. For example, women with nonpalpable tumours detected by mammography, which tend to be smaller and localized, were perhaps more likely to be seen at teaching facilities. Data on screen-detected versus clinically detected tumours were not available to enable finer analysis. There may also be variable referral patterns. However, one would generally expect surgeons in teaching hospitals to receive more complex cases, which may explain the finding that there is no difference in survival for women with larger tumours. On the other hand, women who ask to be or are referred to a teaching hospital, or seek out an academic surgeon, may be in generally better health or have healthier behaviours, resulting in improved survival. Very few of the women in our cohort (2%) were enrolled in clinical trials.

Another possible explanation may be that what is being observed is an artifact of misclassification of cases by disease stage. There were fewer numbers of nodes examined in community hospital cases, which might have led some women with node-positive disease to be misclassified as

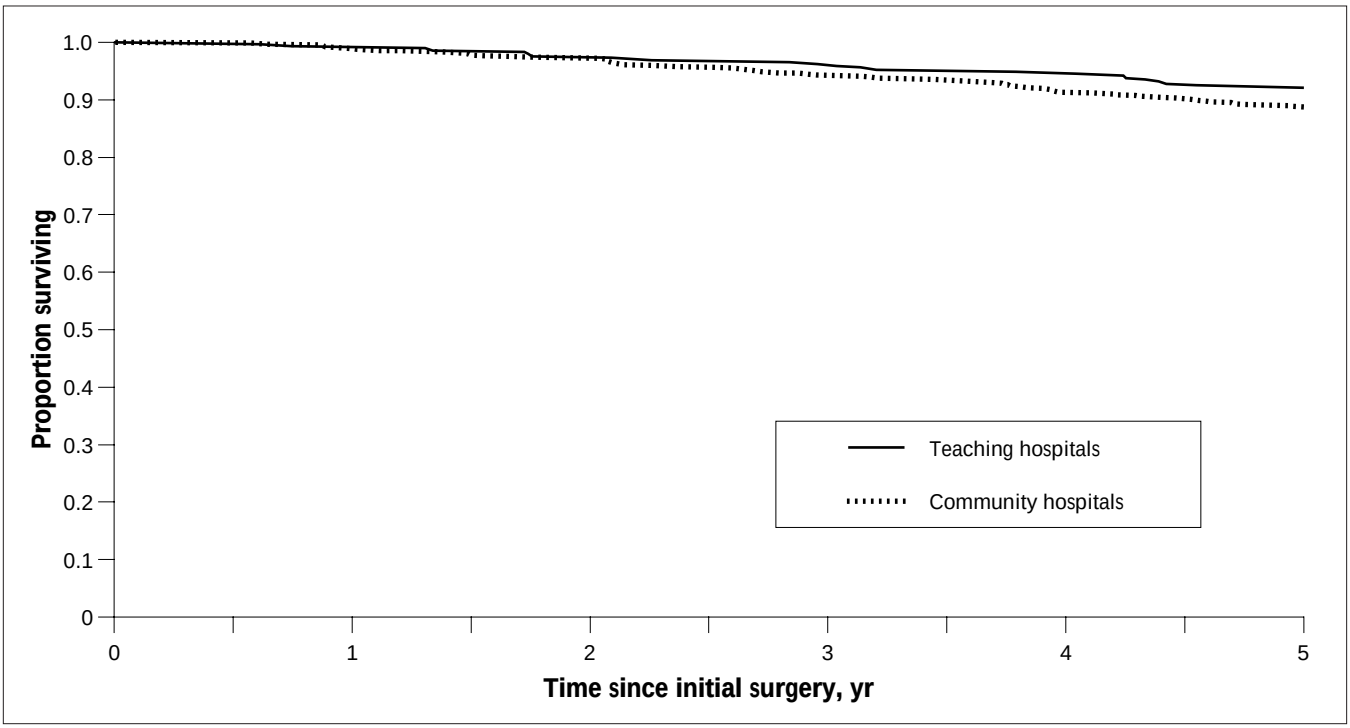

Fig. 1: Kaplan-Meier survival curves for patients by type of hospital at which initial surgery for breast cancer was performed.

node-negative. However, whereas the mean number of nodes examined in the community hospital was lower than that examined in teaching hospitals, it was still high (9.2), making this explanation unlikely. A more subtle bias may have arisen if there were systematic differences in the use of nodal dissection across the 2 types of hospital, given that women with unassessed nodal status were excluded from the study. For example, if community hospitals were more likely to forgo nodal dissections in some cases of clearly localized disease or, conversely, if teaching hospitals were more likely to forgo nodal dissections in cases of more advanced disease, the 2 cohorts would not be as comparable as has been thought. Although it is more likely that nodal dissections would have been forgone in women with more advanced disease, there is no reason to expect evidence to suggest that this would be more likely in teaching hospitals than in community hospitals.

Finally, there may indeed have been subtle differences in the processes of care in the 2 types of hospital, leading to different outcomes. This could include greater use of multidisciplinary teams in the teaching hospitals, with more appropriate use of adjuvant therapy, closer surveillance in follow-up, with a reduction in the number and severity of recurrences, and improved supportive care. Resources available in the teaching hospitals, such as access to specialized breast pathology, may also play a role. This may be reflected in the differences in assessment of tumour grade or estrogen receptors between teaching and community hospitals.

Although the role and skills of the surgeon may be important factors in outcomes for many surgical procedures, they are less likely to be the explanations here. First, breast surgery procedures are not as complex as other procedures where volume–outcome relationships have been observed. Second, we have observed long-term outcomes from breast cancer, and the characteristics of the surgery itself play only a small part in determining the outcome.

Table 4: Results of multivariate analysis

Variable	Relative risk of death (and 95% CI)
Hospital type	
Community	1.00
Teaching	0.47 (0.23–0.96)
Age at diagnosis, yr	
< 50	0.39 (0.23–0.66)
50–65	0.43 (0.27–0.67)
65–90	1.00
Tumour size, mm	
≤ 20	1.00
> 20	1.56 (1.01–2.40)
ER status	
Positive/missing	1.00
Negative	3.16 (2.11– 4.73)
Radiotherapy	
Not received	1.00
Received	0.64 (0.43–0.95)
Interaction between hospital type and tumour size	2.82 (1.13–7.07)

There are several notable limitations to this study. The number of events was small, limiting the study's power. The classification of exposure was done post hoc in a retrospective study. However, it would be difficult to evaluate this hypothesis using an experimental design. We had limited information on comorbidities and other health behaviours that may have affected survival. Finally, there was some missing information on tumour characteristics that may not have been random across the 2 populations.

In conclusion, this study suggests that treatment at teaching centres may be advantageous for women with small tumours. There is a need to identify whether these results can be attributed to differences in specific processes of care. If this is indeed the case, then these processes could be applied in community settings.

Competing interests: None declared.

Contributors: Ms. Chaudhry was the principal author and completed this analysis as part of her MSc degree. She was involved in the data linkage between the original cohort and the mortality data, the review of death certificates, analysis of data and the preparation of the manuscript. Drs. Goel and Sawka were coauthors and coprincipal investigators in the assembly of the cohort of Ontario breast cancer patients, they were responsible for the collection of data about the cohort, and they supervised data linkage and analysis and the preparation of the manuscript. Dr. Goel was Ms. Chaudhry's thesis supervisor and Dr. Sawka was a member of her thesis committee.

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References

1. Iscoe NA, Goel V, Wu K, Fehringer G, Holowaty EJ, Naylor CD. Variation in breast cancer surgery in Ontario. *CMAJ* 1994;150(3):345-52.
2. Goel V, Olivotto I, Hislop TG, Sawka C, Coldman A, Holowaty EJ. Patterns of initial management of node-negative breast cancer in two Canadian provinces. *CMAJ* 1997;156(1):25-35. Abstract available: www.cma.ca/cmaj/vol-156/issue-1/0025.htm
3. Sawka C, Olivotto I, Coldman A, Goel V, Holowaty E, Hislop TG. The association between population-based treatment guidelines and adjuvant therapy for node-negative breast cancer. British Columbia/Ontario Working Group. *Br J Cancer* 1997;75:1534-42.
4. Palda VA, Goel V, Sawka CA. The rise of tamoxifen: temporal and geographical trends of tamoxifen use in Ontario. *Breast Cancer Res Treat* 1997;43:33-41.
5. Whelan T, Marcellus D, Clark R, Levine M. Adjuvant radiotherapy for early breast cancer: patterns of practice in Ontario. *CMAJ* 1993;149(9):1273-7.
6. Hébert-Croteau N, Brisson J, Latreille J, Blanchette C, Deschênes L. Variations in the treatment of early-stage breast cancer in Quebec between 1988 and 1994. *CMAJ* 1999;161(8):951-5. Available: www.cma.ca/cmaj/vol-161/issue-8/0951.htm
7. Luft HS, Hunt SS, Maerki SC. The volume-outcome relationship: practice-makes-perfect or selective-referral patterns? *Health Serv Res* 1987;22:157-82.
8. Farrow DC, Hunt WC, Samet JM. Geographic variation in the treatment of localized breast cancer. *N Engl J Med* 1992;326:1097-101.
9. Nattinger AB, Gottlieb MS, Veum J, Yahnke D, Goodwin JS. Geographic variation in the use of breast-conserving treatment for breast cancer. *N Engl J Med* 1992;326:1102-7.
10. Karjalainen S, Pukkala E. Social class as a prognostic factor in breast cancer survival. *Cancer* 1990;66:819-26.
11. Karjalainen S. Geographical variation in cancer patient survival in Finland: chance, confounding, or effect of treatment? *J Epidemiol Community Health* 1990;44:210-4.
12. Basnett I, Gill M, Tobias JS. Variations in breast cancer management be-

tween a teaching and non-teaching district. *Eur J Cancer* 1992;28A:1945-50.
13. Bonett A, Roder D, Esterman A. Case-survival rates for infiltrating ductal carcinomas by category of hospital at diagnosis in South Australia. *Med J Aust* 1991;154:695-7.
14. Gillis GR, Hole DJ. Survival outcome of care by specialist surgeons in breast cancer: a study of 3786 patients in the west of Scotland. *BMJ* 1996;312:145-8.
15. Sainsbury R, Haward B, Rider L, Johnston C, Round C. Influence of clinician workload and patterns of treatment on survival from breast cancer. *Lancet* 1995;345:1265-70.
16. Lee-Feldstein A, Anton-Culver H, Feldstein PJ. Treatment differences and other prognostic factors related to breast cancer survival. *JAMA* 1994; 271:1163-8.
17. Grilli R, Minozzi S, Tinazzi A, Labianca R, Sheldon TA, Liberati A. Do specialists do it better? The impact of specialization on the processes and outcomes of care for cancer patients. *Ann Oncol* 1998;9:365-74.
18. Holowaty EJ, Marrett LD, Fehringer G. *Cancer incidence in Ontario, trends and regional variations in the 1980's*. Toronto: The Ontario Cancer Treatment and Research Foundation; 1995.
19. Robles SC, Marrett LD, Clarke EA, Risch HA. An application of capture-recapture methods to the estimation of completeness of cancer registration. *J Clin Epidemiol* 1988;41:495-501.
20. Deber R, Thompson GG. Who still prefers aggressive surgery for breast cancer? Implications for the clinical applications of clinical trials. *Arch Intern Med* 1987;147:1543-7.
21. Canadian Hospital Association. *Canadian Hospital Directory 1991–1992*. Ottawa: The Association; 1992.
22. Wilkins R. Use of postal codes and addresses in the analysis of health data. *Health Rep* 1993;5:157-77.
23. Clarke EA, Marrett LD, Kreiger N. *Twenty years of cancer incidence, 1964–1983: the Ontario Cancer Registry*. Toronto: The Ontario Cancer Treatment and Research Foundation; 1987.
24. World Health Organization. *International classification of diseases*. 9th rev. ed. Geneva: The Organization; 1978.

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