

# Appropriate treatment receipt after breast-conserving surgery

K. Guidolin MD,\* M. Lock MD,<sup>†‡</sup> K. Vogt MD MSc,<sup>†‡</sup> J.A. McClure MSc,<sup>§</sup> J. Winick-Ng MSc,<sup>§</sup> C. Vinden MD,<sup>†‡§</sup> and M. Brackstone MD PhD<sup>†‡</sup>

# ABSTRACT

**Background** Breast-conserving surgery (BCS) and radiation therapy (RT) are the standard of care for early breast cancer, although some women receive ipsilateral mastectomy or adjuvant tamoxifen, both of which can be appropriate alternatives to RT. Objectives of the present study were to determine the proportion of women who are treated appropriately after BCS and to identify factors associated with non-receipt of RT.

**Methods** This retrospective cohort study used Ontario data linked at the Institute for Clinical and Evaluative Sciences to examine 33,718 patients who received Bcs during 2004–2010. Primary outcome was RT receipt. The ipsilateral mastectomy rate and patient, surgeon, and setting variables were measured.

**Results** Of the study patients, 86.1% received either RT or completion mastectomy; in the cohort less than 70 years of age, 90.8% received RT or completion mastectomy. Among patients less than 70 years of age, 3 risk factors for non-receipt of RT were identified: age less than 46 years, treatment in a non-academic institution, and earlier year of initial BCS. Additionally, in the overall cohort, RT non-receipt was associated with high comorbidity, more than 40 km to the cancer centre, income quintile, and breast care specialization.

**Conclusions** In Ontario, 90.8% of patients less than 70 years of age are appropriately treated for early breast cancer; approximately 1 in 10 do not receive RT or completion mastectomy. Based on those findings, women less than 46 years of age might be at increased risk of recurrence and death because of incomplete treatment. It also appears that academic centres more effectively treat breast cancer; however, breast cancer care appears to be improving over time in Ontario.

Key Words Radiation, breast cancer, surgery

Curr Oncol. 2018 Dec;25(6):e545-e552

www.current-oncology.com

# **INTRODUCTION**

Breast-conserving therapy consists of breast-conserving surgery (BCS), wherein the primary tumour is excised, retaining a reasonable breast volume and shape, followed by adjuvant radiotherapy (RT). Breast-conserving therapy for early-stage breast cancer has been shown in long-term multicentre trials (level I evidence) to be equivalent to mastectomy in terms of survival<sup>1–10</sup>. With BCS alone (without RT), the risk of ipsilateral recurrence is increased by a factor of 3<sup>11</sup>; therefore, for most patients, the use of RT after BCS is imperative if breast-conserving therapy is to be considered a standard of care for nonmetastatic breast cancer<sup>12</sup>.

Despite clear guidelines, use of RT after BCS varies widely from 66% to 99%, based on Canadian and U.S.

data<sup>13,14</sup>. Several studies have examined RT uptake after BCS; however, those studies did not take into account two appropriate alternatives to adjuvant RT: ipsilateral ("completion") mastectomy, or adjuvant tamoxifen for patients more than 70 years of age to reduce the local recurrence risk<sup>15</sup>. Completion mastectomy might be chosen after an initial BCS because of a positive resection margin or discovery of further disease. In addition, some patients might elect mastectomy upon consultation with a radiation oncologist. When a patient undergoes mastectomy, adjuvant radiation might no longer be beneficial. A study published in 2004 established that, for patients 70 years of age and older, BCS with adjuvant tamoxifen therapy alone is acceptable treatment for early-stage breast cancer<sup>15</sup>. Patients who have received adjuvant RT, completion

**Correspondence to:** Keegan Guidolin, 2075 Bayview Avenue, Room H317, Toronto, Ontario M4N 3M5. E-mail: keegan.guidolin@mail.utoronto.ca **DOI:** https://doi.org/10.3747/co.25.4117 **Supplemental material available at http://www.current-oncology.com**  mastectomy, or tamoxifen therapy (older patients with low-risk early-stage cancers) should all be considered to have been appropriately treated.

Several studies have examined factors associated with receipt of RT after BCS. Many of the associations reported by those studies are contradictory, which could indicate that the relevant factors are population-dependent. The factors most commonly associated (whether positively or negatively) with RT receipt include age, comorbidity burden, treatment at an academic centre, and residence in a rural location<sup>13,16–20</sup>. Many other factors have been less consistently associated with RT receipt in some smaller studies, including clinical stage or grade, tumour size, nodal or estrogen receptor status, presence of *in situ* disease, non-receipt of concurrent chemotherapy, relationship status, and ethnicity<sup>13,16–20</sup>.

A large-scale Canadian study that includes consideration of alternative treatment plans after BCS, including RT, hormonal therapy, and completion mastectomy is needed. Differences between the U.S. and Canadian systems limit the generalizability of U.S. studies to the early-stage population, in particular because health insurance status is often cited as a major factor in RT receipt<sup>13,16,21</sup>. To understand barriers limiting access to appropriate treatment, the objectives of the present study were to determine the proportion of women with breast cancer who receive RT or completion mastectomy after BCs compared with all those who undergo BCs, and to identify patient, procedure, and surgeon factors associated with failure to receive RT after BCS. Given that prescription drug data for women less than 65 years of age in Ontario with drug plans are not comprehensive for our study period, and given that many studies have demonstrated poor compliance with hormonal therapy when prescribed, we chose not to address tamoxifen use as an alternative to RT in this study.

# **METHODS**

# **Study Setting and Design**

Residents of the province of Ontario (2017 population: 14.19 million)<sup>22</sup> have access to universal health care, and their interactions with hospital and physician services are recorded in administrative databases. Relevant datasets were linked using unique encoded identifiers and were analyzed at the Institute for Clinical Evaluative Sciences (ICES) Western site. All reporting follows the RECORD (Reporting of Studies Conducted Using Observational Routinely-Collected Health Data) statement (supplementary Table 1).

Our retrospective cohort study included all patients with a new diagnosis of breast cancer (Ontario Cancer Registry) who underwent BCS in Ontario between 1 April 2004 and 31 March 2010 in the initial cohort. The definition of BCS was a hospital procedure code for breast lumpectomy concurrent with an OHIP (Ontario Health Insurance Program) physician billing code for BCS. To accommodate for patients given neoadjuvant chemotherapy, patients were included in the cohort if they underwent surgery (OHIP physician billing code and Canadian Classification of Health Interventions procedure code within 2 days of each other) within 12 months of diagnosis. To capture data for physician-specific covariates, we limited our cohort to patients with both a Canadian Classification of Health Interventions and an OHIP code. In a stepwise manner, these exclusion criteria were applied: male sex; age less than 16 years or greater than 105 years; non-Ontario residence; no physician billing record for BCS within 2 days of the procedure date; breast cancer diagnosis more than 1 year before BCS; Hodgkin lymphoma (the most likely cause for non-breast RT to the chest); previous lumpectomy or mastectomy (to exclude patients likely to have previously been irradiated); history of lupus, scleroderma, or dermatomyositis (relative contraindications to radiation); prior RT; and unknown laterality (for index BCS). Figure 1 shows the cohort build, and a complete list of the codes used can be found in supplementary Table 2. Table I shows baseline variables for the final cohort.

## **Data Sources**

Data were obtained from 7 linked Ontario databases: the Discharge Abstract Database and Same Day Surgery database maintained by the Canadian Institute for Health Information (CIHI), the National Ambulatory Care Reporting System database, the OHIP claims database, the Registered Persons Database, the ICES physician database, and the Ontario Cancer Registry. For details, see supplementary Table 3.

## Outcomes

The primary outcomes for the study were evidence of RT consultation (using OHIP billing codes for RT consultation) and RT receipt (using OHIP billing codes for RT planning), within 1 year of BCS (to include patients requiring adjuvant chemotherapy before RT). Secondary outcomes included repeat BCS or completion mastectomy on the ipsilateral side. "Completion mastectomy" was defined as a mastectomy performed within 1 year after an initial BCS (presumed to have been done for the same indication). A completion mastectomy is typically done when the initial BCS was unable to achieve negative margins or when the patient is found to be a carrier of a hereditary breast cancer (*BRCA*) gene mutation. The time window of 1 year



**FIGURE 1** Cohort creation. Suppressed values (NR) are added to the next reportable field. OHIP = Ontario Health Insurance Plan.

allowed for completion of adjuvant chemotherapy before further surgery.

TABLE I E	Baseline	characteristics	of the	study	cohort
-----------	----------	-----------------	--------	-------	--------

Characteristic	Value
Patients (n)	22,032
Age (years)	
Mean	59.6±13.1
Median	59.0
IQR	50.0-69.0
Rural residence [n (%)]	2684 (12.2)
Income quintile [n (%)]	
Missing	70 (0.3)
Quintile 1	3,700 (16.8)
Quintile 2	4,199 (19.1)
Quintile 3	4,351 (19.7)
Quintile 4	4,767 (21.6)
Quintile 5	4,945 (22.4)
Resource utilization band [n (%)]	
Low	10,217 (46.4)
Moderate	7,695 (34.9)
High	4,120 (18.7)
Nearest cancer centre (km)	
Mean	31.1±57.9
Median	17.4
IQR	5.0-27.6
Time from diagnosis to lumpectomy (days)	
Mean	28.6±31.3
Median	25.0
IQR	11.0-38.0
Laterality [n (%)]	
Bilateral	302 (1.4)
Left	10,958 (49.7)
Right	10,772 (48.9)
Teaching hospital [n (%)]	5,042 (22.9)
Prior RT consultation [n (%)]	69 (0.3)
Fiscal year [n (%)]	
2004	3,400 (15.4)
2005	3,693 (16.8)
2006	3,818 (17.3)
2007	3,687 (16.7)
2008	3,642 (16.5)
2009	3,792 (17.2)

# Patient, Surgeon, and Treatment Variables

Patient variables included age, rural residence ("rurality"), socioeconomic status (estimated using neighbourhood income quintile), expected resource utilization (an estimate of comorbidity), distance from home to the nearest cancer centre, time from cancer diagnosis to surgery, and surgery laterality (right vs. left BCs). Stage was a desired variable to confirm that most patients in this cohort had early-stage disease, for which BCs followed by radiation is most typically offered as the standard of care; however, staging information was available for only 51% of the patients and for only a portion of the study period. Of the patients for whom stage was available, 91% had early-stage disease (stage 0, I, or II), suggesting that the overall cohort represented our desired patient population. Our cohort reflected the clinical reality that a small number of patients seen at surgical consultation with clinically early disease end up having more nodal involvement than expected or distant metastases on imaging, resulting in upstaging.

We determined patient comorbidity using the Johns Hopkins Adjusted Clinical Groups system score (version 10: used with permission)<sup>23</sup>. This method of case-mix grouping captures all morbidities for which a patient receives care during a defined period—in this case, 2 years before the procedure date. The Adjusted Clinical Groups can be collapsed into 6 resource utilization bands (RUBS) on the basis of expected use of health care resources. In the present study, we used the Discharge Abstract Database, the Same Day Surgery database, the National Ambulatory Care Reporting System, and OHIP databases to calculate RUBS, which were summarized as a 3-point ordinal variable: 1 =low (RUB 0–3), 2 = moderate (RUB 4) and 3 = high (RUB 5).

Surgeon variables included age, sex, and breast specialization. Breast specialization was calculated as a continuous variable, determined by dividing the number of breast-related consultations by the total number of consultations conducted by the surgeon during the fiscal year in question, reflecting the proportion of all patient referrals to a given surgeon that were specifically breast-focused in nature. Treatment variables included setting of the surgery (teaching vs. community hospital), and fiscal year of the surgery.

# **Statistical Analysis**

Log binomial regression was used to find associations between predictor variables and RT planning, with results reported as relative risk (RR) with 95% confidence interval (CI). Potential predictor variables included patient age, income quintile, patient comorbidity (RUB), rurality, distance to cancer centre, surgeon age, breast specialization, hospital setting, and fiscal year. Generalized estimating equations were used to account for the clustering of patients within physicians and hospitals. The linearity of continuous predictors was assessed using restricted cubic splines<sup>24</sup>. Continuous variables that demonstrated a nonlinear association with the dependent variable were categorized before modelling. A subgroup analysis using the same methodology was also conducted to investigate predictors of RT planning in patients less than 70 years of age, because older patients could have other reasons for not receiving RT, such as competing comorbidities or use of tamoxifen not captured in the current study. All analyses were conducted using the SAS software application (version 9.3, PROC GENMOD: SAS Institute, Cary, NC, U.S.A.).

## **Ethics Approval**

The study was approved by the Sunnybrook Health Sciences Centre Research Ethics Board.

# RESULTS

The initial cohort size was 33,718 patients. After the exclusion criteria were applied, the total number of patients included was 22,032.

The proportions of patients attending a RT consultation, receiving RT, and receiving RT or completion mastectomy are shown in Table II, overall and by age (<70 or  $\geq$ 70 years). Of the 22,032 patients included in the cohort, 18,976 patients (86.1%) received either RT or completion mastectomy. Of the 16,734 patients less than 70 years of age, 15,201 (90.8%) received RT or completion mastectomy, and of the 5294 patients 70 years of age and older, 3772 (71.3%) received either RT or completion mastectomy. Table II also shows data for the cohort by age decade, demonstrating that the lowest rate of treatment in patients less than 70 years of age occurred in the youngest group (<30 years).

Table III shows results of the analysis for risk factors associated with RT for the cohort overall and for patients less than 70 years of age (Table IV shows quintile information). The RRs obtained represent the risk of not receiving RT, which we considered to be incomplete treatment. Patients were considered to have been incompletely treated if they received surgery but not adjuvant RT. (Note that the term "incomplete treatment" is not meant to be a reflection of the clinical appropriateness or adequacy of the treatment plan.)

Patient age was significantly associated with RT receipt in both groups. The patients less than 70 years of age who were least likely to receive incomplete treatment were those between 46 and 56 years of age (quintile 2 RR:

#### TABLE II Radiotherapy outcomes

0.82; p = 0.0002; quintile 3 RR: 0.81; p = 0.0001). Patients less than 46 years of age (quintile 1) and 63–70 years of age (quintile 5) received RT at approximately the same rate (RR: 0.96; p = 0.395).

Compared with patients treated in community hospitals, those treated in academic hospitals were less likely to be incompletely treated in both the overall cohort (RR: 0.86; p = 0.013) and in the group less than 70 years of age (RR: 0.82; p = 0.008). Both groups showed a decreased risk of incomplete treatment over time (overall cohort RR: 0.84; p = 0.001; patients less than 70 years of age RR: 0.83; p = 0.009).

Further associations were found in the overall cohort, but not for patients less than 70 years of age (Table III). Incomplete treatment was more likely for patients with a high comorbidity burden than for those with few or no comorbidities (RR: 1.22; p < 0.0001). It was also more likely for patients who lived more than 40 km from the cancer centre than for those living closer than 40 km (RR: 1.11; p = 0.037). Patient income quintile was significantly associated with RT receipt such that incomplete treatment was less likely for those in the highest income quintile than for those in the lowest income quintile (RR: 0.90; p = 0.013). Patients were also at increased risk of not receiving RT if the surgeon who performed the BCS was in the lowest quintile of breast specialization.

# DISCUSSION

Patients who undergo BCS usually require adjuvant RT. We considered two methods of evaluating patient involvement with RT after BCS for breast cancer: whether patients received a consultation with a radiation oncologist, and whether patients received RT, as evidenced by RT planning.

To more accurately identify the proportion of women with breast cancer having BCS without adjuvant RT, we were interested in capturing those who had received RT or completion mastectomy after BCS. Overall, 17,358 patients in the cohort (78.79%) received RT, and an additional 1618

Age group	Pts	Outcome [ <i>n</i> (%)]					
	( <b>n</b> )	Consultation	Planning	Planning or mastectomy			
Overall	22,032	19,334 (87.75)	17,358 (78.79)	18,976 (86.13)			
<70 Years	16,736	15,215 (90.91)	13,950 (83.35)	15,203 (90.84)			
≥70 Years	5,296	4,119 (77.78)	3,408 (64.35)	3,773 (71.24)			
<30 Years	105	96 (91.43)	80 (76.19)	93 (88.57)			
30–39 Years	989	891 (90.09)	793 (80.18)	893 (90.29)			
40–49 Years	4,265	3,843 (90.11)	3,545 (83.12)	3,912 (91.72)			
50–59 Years	5,981	5,495 (91.87)	5,087 (85.05)	5,495 (91.87)			
60–69 Years	5,396	4,890 (90.62)	4,445 (82.38)	4,810 (89.14)			
70–79 Years	3,575	3,080 (86.15)	2,680 (74.97)	2,955 (82.66)			
80–89 Years	1,511	993 (65.72)	712 (47.12)	800 (52.95)			
≥90 Years	210	46 (21.9)	16 (7.62)	17-21 (8-10)			

Pts = patients.

patients (7.34%) underwent completion mastectomy. Given guidelines to support the use of adjuvant tamoxifen instead of radiation for estrogen receptor–positive cancers in women more than 70 years of age, we also looked at the subset of patients in our cohort who were less than 70 years of age (for whom radiation would be considered standard of care). Of the 16,734 patients less than 70 years of age, 15,201 had RT planning or mastectomy; 90.8% of patients

TABLE III	Results from log binomial	regression predictir	ng failure to receive	radiotherapy planning	g within 1	year of lumpectomy
-----------	---------------------------	----------------------	-----------------------	-----------------------	------------	--------------------

Parameter and comparator	Adjusted							
	All patients (n=22,032)				Patients <70 years of age ( <i>n</i> =16,734)			
	Estimate	95% Cl		р	Estimate	95% CI		p
		Lower	Upper	Value		Lower	Upper	Value
Patient age quintile <sup>a</sup>								
2 vs. 1	0.873	0.796	0.959	0.0043	0.820	0.739	0.910	0.0002
3 vs. 1	0.899	0.813	0.993	0.0354	0.809	0.727	0.901	0.0001
4 vs. 1	1.047	0.949	1.154	0.3592	0.886	0.794	0.987	0.0285
5 vs. 1	2.124	1.941	2.325	< 0.0001	0.957	0.864	1.060	0.3952
Income quintile <sup>a</sup>								
2 vs. 1	0.942	0.863	1.027	0.1763	1.024	0.909	1.153	0.6987
3 vs. 1	0.965	0.884	1.053	0.4272	0.956	0.845	1.082	0.4776
4 vs. 1	0.931	0.860	1.007	0.0756	0.914	0.814	1.025	0.1251
5 vs. 1	0.901	0.830	0.978	0.0129	0.911	0.811	1.023	0.1155
Resource utilization band								
2 vs. 1	1.044	0.985	1.107	0.1471	0.992	0.919	1.071	0.8386
3 vs. 1	1.222	1.146	1.303	< 0.0001	1.062	0.961	1.174	0.2377
Rural								
Yes vs. no	1.045	0.940	1.163	0.4128	1.083	0.947	1.238	0.2463
Distance								
≤40 km vs. >40 km	1.110	1.007	1.224	0.0365	1.116	0.991	1.256	0.0694
Surgeon age quintileª								
2 vs. 1	0.987	0.896	1.088	0.7982	0.929	0.825	1.045	0.2199
3 vs. 1	1.036	0.927	1.158	0.5331	0.960	0.835	1.105	0.5696
4 vs. 1	1.021	0.923	1.130	0.6875	0.969	0.857	1.095	0.6095
5 vs. 1	1.093	0.983	1.215	0.1012	1.045	0.906	1.205	0.5460
Breast devotion quintile <sup>a,b</sup>								
2 vs. 1	0.934	0.844	1.034	0.1858	0.955	0.835	1.092	0.4997
3 vs. 1	0.879	0.783	0.986	0.0273	0.878	0.756	1.019	0.0858
4 vs. 1	0.858	0.756	0.973	0.017	0.973	0.838	1.129	0.7151
5 vs. 1	0.846	0.728	0.984	0.0295	0.933	0.761	1.144	0.5052
Teaching hospital (yes vs. no)	0.861	0.766	0.968	0.0125	0.817	0.702	0.949	0.0084
Fiscal year								
2005 vs. 2004	1.030	0.948	1.120	0.4817	0.982	0.869	1.110	0.7749
2006 vs. 2004	0.951	0.872	1.037	0.2595	0.942	0.835	1.064	0.3365
2007 vs. 2004	0.906	0.824	0.997	0.044	0.956	0.845	1.082	0.4779
2008 vs. 2004	0.859	0.783	0.942	0.0012	0.874	0.769	0.993	0.0392
2009 vs. 2004	0.839	0.756	0.931	0.0009	0.827	0.718	0.954	0.0090

<sup>a</sup> See Table IV for quintile specifications.

<sup>b</sup> The number of breast-related billing codes (consults, procedures, etc.) as a proportion of the total number of billing codes used by an individual surgeon.

#### TABLE IV Quintile specifications

Variable	Quintile						
	1	2	3	4	5		
Age (years)	<48	48–54	55-62	63–71	≤72		
Surgeon age (years)	<40	40-45	46–50	51–56	≤57		
Breast specialization <sup>a</sup> (%)	<6.57	6.57-13.01	13.02-23.54	23.55-42.24	≤42.25		
Age <70 years (years)	<46	46–51	52–56	57–62	≤63		
Age $\geq$ 70 years (years)	<72	72–74	75–77	78-81	≤81		

<sup>a</sup> The number of breast-related billing codes (consults, procedures, etc.) as a proportion of the total number of billing codes used by an individual surgeon.

with early-stage breast cancer can therefore be considered to have been treated appropriately.

Although that percentage is high, when the high prevalence of breast cancer is considered, our results suggest that almost 10% of patients are not receiving standard-of-care therapy, which puts them at significantly increased risk of recurrence<sup>11</sup>. The issue is one of health care resource use, in that an expense is attached to treatment of the resulting recurrences, not to mention the consequences for the patient of an increased risk of distant metastasis and death associated with a recurrence.

Three factors were found to be significantly associated with RT receipt in the cohort of patients less than 70 years of age: age, surgical treatment in an academic hospital, and year of surgery. The youngest patients in that group, those less than 46 years of age, were at greatest risk of not receiving RT. Some of those women go on to receive mastectomy; however, even within the cohort of patients less than 70 years of age, approximately 10% of women less than 46 years of age are receiving BCs alone. Unfortunately, without RT or mastectomy, those women are not only at increased risk of ipsilateral recurrence, but they also experience just one third the overall survival experienced by those who receive appropriate treatment<sup>25</sup>. Previous studies have hypothesized that women do not receive RT because of their childcare commitments<sup>16</sup>. That hypothesis clearly identifies a barrier that could be addressed with interventions such as funded childcare programs run out of cancer centres for such patients.

Surgical treatment in an academic centre was found to be associated with receipt of appropriate treatment, a finding that accords with results reported in prior studies<sup>26</sup>. We were unable to determine whether patients treated in the community were never referred to a radiation oncologist or whether the referral was somehow lost. It might be the case that academic hospitals are more successful in treating these patients because the hospitals are more likely to use a multidisciplinary team approach that includes radiation oncologists, physicists, and technologists in addition to the medical and surgical teams to coordinate care.

The proportion of patients appropriately treated increased over the course of the study, indicating that overall breast cancer care delivery is improving in Ontario over time.

A number of additional factors that were significantly associated with whether patients in the overall cohort

received RT were nonsignificant in the group less than 70 years of age, indicating that the older population (some of whom might have been treated with adjuvant tamoxifen) drives those associations. Those factors included age, comorbidity burden, income, and distance from the cancer centre, all of which have been identified as significant in other studies<sup>13,15–20</sup>. Greater breast case volume for the surgeon also predicted RT receipt. That observation suggests that older patients might require more counselling and advocacy from their physician to ensure that they are selecting a treatment option that is appropriate for their current state of health. Recent data suggest that, of patients who do not receive RT, up to 7% do not receive it because they are deemed medically unfit by their radiation oncologist<sup>27</sup>. We suggest that greater success could be achieved if patients selected for breast-conserving therapy are seen by a radiation oncologist preoperatively rather than postoperatively to ensure that the patient is appropriately informed, prepared, and medically fit to undergo RT before the breast-conserving therapy begins.

Undergoing surgery by a surgeon who treats a higher volume of breast disease was found to be significantly associated with increased likelihood of receiving a radiation oncology consultation, which might also be explained by improved communication with radiation oncologists or increased awareness of the necessity of RT for appropriate disease management.

# Limitations

A potential limitation of the present study is the administrative nature of its databases, particularly the OHIP billing code database. Billing practices vary between physicians, and there are many reasons that RT consultations or planning might not be billed. Incorrect billing codes and forgotten billing are examples. The rate of missed billings has been estimated to be at least 5%<sup>28</sup>.

Another limitation is the inability to discern whether a patient actually received the complete course of RT. The most direct measure that exists in the relevant databases is the OHIP codes for treatment planning in conjunction with multiple radiation visits; however, even that conjunction of data assumes that every patient who received planning not only started treatment, but also successfully completed it. That method likely overestimates the proportion of patients who successfully receive a complete course of adjuvant RT. Our study included a subgroup analysis of patients less than 70 years of age, given that patients older than 70 could be appropriately treated with adjuvant tamoxifen alone. Because we did not have reliable estimates of tamoxifen use for all patients in the cohort, and because breast cancer patients are reported to have low rates of compliance with hormonal therapy, we did not include estimates of tamoxifen use in the study. If anything, an analysis of tamoxifen use would overestimate the number of women appropriately treated. Thus, our conclusions represent a conservative illustration of the proportion of breast cancer patients who do not receive standard-of-care treatment for their disease.

Table III describes the risk factors predicting non-receipt of RT; however, the regression analysis includes patients who ultimately went on to have a mastectomy. It would have been interesting to parse the latter patients out; however, their retention is a limitation of our databases.

We were unable to address the influence that pregnancy (a relative contraindication to RT) might have had on rates of RT receipt (which could be particularly important in younger women), because pregnancy is not coded in the databases we used. However, pregnant patients typically present with at least T2 disease and therefore typically receive neoadjuvant or adjuvant chemotherapy. By the time chemotherapy is completed, the pregnancy would also have been completed and would therefore not preclude RT within 12 months of surgery. We do not feel that this group represents a major limitation in our study.

# **CONCLUSIONS**

This is the first large-scale study to estimate adjuvant therapy receipt (RT or completion mastectomy) in patients after BCS. The results demonstrate that a significant proportion of Ontario women do not receive appropriate treatment for their early-stage breast cancer, with about 10% of women, or 1 in 10 patients, not receiving RT or mastectomy. Compared with older patients, those less than 46 years of age were found particularly to experience incomplete treatment, which could put them at increased risk of recurrence and death. Although avoiding radiation is appropriate in select patients (such as those more than 70 years of age, who can receive tamoxifen instead; or those with significant comorbidities), we found that patients were more likely to be treated appropriately if they were treated in academic hospitals rather than in community hospitals, and that overall rates of RT receipt seemed to improve with time. Interventions aimed at improving education and access to RT for all patients, particularly younger women, could dramatically improve breast cancer care delivery in Ontario.

#### ACKNOWLEDGMENTS

This study was supported by the ICES Western site. Funding for ICES comes in the form of an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). Core funding for ICES Western is provided by the Academic Medical Organization of Southwestern Ontario (AMOSO), the Schulich School of Medicine and Dentistry (SSMD), Western University, and the Lawson Health Research Institute (LHRI). The opinions, results, and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES, AMOSO, SSMD,

LHRI, or the Ontario MOHLTC is intended or should be inferred. Parts of this material are based on data or information compiled and provided by CIHI. However, the analyses, conclusions, opinions, and statements expressed in the material are those of the authors and not necessarily those of CIHI. Parts of this material are based on data and information provided by Cancer Care Ontario (cco). The opinions, results, views, and conclusions reported in this paper are those of the authors and do not necessarily reflect those of cco. No endorsement by cco is intended or should be inferred.

## CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

## AUTHOR AFFILIATIONS

\*Department of Surgery, University of Toronto, Toronto, <sup>†</sup>Schulich School of Medicine and Dentistry, Western University, London, <sup>‡</sup>London Health Sciences Centre, London, and <sup>§</sup>Institute for Clinical Evaluative Sciences, London, ON.

#### REFERENCES

- 1. Fisher B, Anderson S, Redmond CK, Wolmark N, Wickerham DL, Cronin WM. Reanalysis and results after 12 years of followup in a randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* 1995;333:1456–61.
- 2. Fisher B, Anderson S, Bryant J, *et al.* Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;347:1233–41.
- 3. Veronesi U, Salvadori B, Luini A, *et al.* Breast conservation is a safe method in patients with small cancer of the breast. Long-term results of three randomised trials on 1,973 patients. *Eur J Cancer* 1995;31A:1574–9.
- Veronesi U, Cascinelli N, Mariani L, *et al.* Twenty-year followup of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002;347:1227–32.
- 5. van Dongen JA, Voogd AC, Fentiman IS, *et al.* Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. *J Natl Cancer Inst* 2000;92:1143–50.
- 6. Jacobson JA, Danforth DN, Cowan KH, *et al*. Ten-year results of a comparison of conservation with mastectomy in the treatment of stage I and II breast cancer. *N Engl J Med* 1995;332:907–11.
- 7. Poggi MM, Danforth DN, Sciuto LC, *et al.* Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial. *Cancer* 2003;98:697–702.
- Arriagada R, Lê MG, Rochard F, Contesso G. Conservative treatment versus mastectomy in early breast cancer: patterns of failure with 15 years of follow-up data. Institut Gustave-Roussy Breast Cancer Group. J Clin Oncol 1996;14:1558–64.
- 9. Blichert-Toft M, Rose C, Andersen JA, *et al.* Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life-table analysis. Danish Breast Cancer Cooperative Group. *J Natl Cancer Inst Monogr* 1992;:19–25.
- 10. Clarke M, Collins R, Darby S, *et al.* on behalf of the Early Breast Cancer Trialists' Collaborative Group. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005;366:2087–106.
- 11. Vinh-Hung V, Verschraegen C. Breast-conserving surgery with or without radiotherapy: pooled-analysis for risks of ipsilateral breast tumor recurrence and mortality. *J Natl Cancer Inst* 2004;96:115–21.

- Cancer Care Ontario (cco), Practice Guidelines Initiative. Breast Irradiation in Women with Early Stage Invasive Breast Cancer Following Breast Conserving Surgery. Toronto, ON: cco; 1997. [Available online at: http://www.breastsurgeonsweb. com/wp-content/uploads/downloads/2012/10/305.pdf; cited 12 December 2016]
- 13. Dragun AE, Huang B, Tucker TC, Spanos WJ. Disparities in the application of adjuvant radiotherapy after breast-conserving surgery for early stage breast cancer: impact on overall survival. *Cancer* 2011;117:2590–8.
- 14. Fiorica F, Berretta M, Ursino S, *et al.* Adjuvant radiotherapy on older and oldest breast cancer patients after conservative surgery: a retrospective analysis. *Arch Gerontol Geriatr* 2012;55:283–8.
- 15. Hughes KS, Schnaper LA, Bellon JR, *et al.* Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. *J Clin Oncol* 2013;31:2382–7.
- 16. Pan IW, Smith BD, Shih YC. Factors contributing to underuse of radiation among younger women with breast cancer. *J Natl Cancer Inst* 2014;106:djt340.
- Showalter SL, Grover S, Sharma S, Lin L, Czerniecki BJ. Factors influencing surgical and adjuvant therapy in stage I breast cancer: a SEER 18 database analysis. *Ann Surg Oncol* 2013;20:1287–94.
- Tuttle TM, Jarosek S, Habermann EB, Yee D, Yuan J, Virnig BA. Omission of radiation therapy after breast-conserving surgery in the United States: a population-based analysis of clinicopathologic factors. *Cancer* 2012;118:2004–13.
- Adegboyega TO, Landercasper J, Linebarger JH, *et al.* Institutional review of compliance with NCCN guidelines for breast cancer: lessons learned from real-time multidimensional synoptic reporting. *J Natl Compr Canc Netw* 2015;13:177–83.
- 20. Wheeler SB, Wu Y, Meyer AM, *et al.* Use and timeliness of radiation therapy after breast-conserving surgery in low-income women with early-stage breast cancer. *Cancer Invest* 2012;30:258–67.

- 21. Ramsey SD, Zeliadt SB, Richardson LC, *et al.* Discontinuation of radiation treatment among Medicaid-enrolled women with local and regional stage breast cancer. *Breast J* 2010;16:20–7.
- 22. Statistics Canada. Population estimates on July 1st, by age and sex [table 17-10-0005-01]. Ottawa, ON: Statistics Canada; 2018. [Available online at: http://www.statcan.gc.ca/ tables-tableaux/sum-som/l01/cst01/demo02a-eng.htm; cited 13 October 2018]
- 23. *The Johns Hopkins ACG Case-Mix System: Version 6.0 Release Notes.* Baltimore, MD: The Johns Hopkins University Bloomberg School of Public Health; 2003.
- Fang J, Austin PC, Tu JV. Test for linearity between continuous explanatory and binary outcome first, run a multivariate regression analysis second. Toronto, ON: SAS Global Forum; 2009. [Available online at: http://support.sas.com/resources/ papers/proceedings09/252-2009.pdf; cited 12 September 2017]
- 25. Park HL, Chang J, Lal G, Lal K, Ziogas A, Anton-Culver H. Trends in treatment patterns and clinical outcomes in young women diagnosed with ductal carcinoma *in situ*. *Clin Breast Cancer* 2018;18:e179–85.
- 26. Komenaka IK, Pennington RE Jr, Schneider BP, *et al.* Compliance differences between patients with breast cancer in university and county hospitals. *Clin Breast Cancer* 2010;10:385–91.
- 27. Guidolin K, Lock M, Brackstone M. Patient-perceived barriers to radiation therapy for breast cancer. *Can J Surg* 2017;61:15716.
- 28. Canadian Medical Association (CMA). *Module 8: Physician Remuneration Options*. Ottawa, ON: MD Physician Services, CMA; 2012. [Available online at: https://www.cma.ca/Assets /assets-library/document/en/practice-management-and-wellness/module-8-physician-remuneration-options-e. pdf; cited 20 November 2016].