Comparison of wait times across the breast cancer treatment pathway among screened women undergoing organized breast assessment versus usual care

Kristina M. Blackmore¹ · Ashini Weerasinghe¹ · Claire M. B. Holloway^{2,3} · Vicky Majpruz¹ · Lucia Mirea^{4,5} · Frances P. O'Malley⁶ · Cathy Paroschy Harris⁷ · Ashley Hendry⁸ · Amanda Hey⁹ · Anat Kornecki¹⁰ · George Lougheed¹¹ · Barbara-Anne Maier¹² · Patricia Marchand¹³ · David McCready^{3,14} · Carol Rand¹⁵ · Simon Raphael¹⁶ · Roanne Segal-Nadler¹⁷ · Neelu Sehgal¹⁸ · Derek Muradali^{1,19,20} · Anna M. Chiarelli^{1,5}

Received: 17 October 2018 / Accepted: 28 March 2019 / Published online: 29 April 2019
© The Canadian Public Health Association 2019

Abstract

Objective The benefit of organized breast assessment on wait times to treatment among asymptomatic women is unknown. The Ontario Breast Screening Program (OBSP) offers screening and organized assessment through Breast Assessment Centres (BAC). This study compares wait times across the treatment pathway among screened women diagnosed with breast cancer through BAC and usual care (UC).

Methods A retrospective design identified two concurrent cohorts of postmenopausal women aged 50–69 within the OBSP diagnosed with screen-detected invasive breast cancer and assessed in BAC ($n = 2010$) and UC ($n = 1844$) between 2002 and 2010. Demographic characteristics were obtained from the OBSP. Medical chart abstraction provided prognostic and treatment data. Multinomial logistic regression examined associations of assessment type with wait times from abnormal mammogram to surgery, chemotherapy or radiotherapy.

Results Compared with through UC, postmenopausal women diagnosed through BAC were significantly less likely to have longer wait times (days) from an abnormal mammogram to definitive surgery (> 89 vs. ≤ 47 ; OR = 0.63; 95% CI = 0.52–0.77), from final surgery to radiotherapy (> 88 vs. ≤ 55 ; OR = 0.71; 95% CI = 0.54–0.93) and from final chemotherapy to radiotherapy (> 41 vs. ≤ 28 ; OR = 0.52; 95% CI = 0.36–0.76). Conversely, women assessed through BAC compared with through UC were more likely to experience longer wait times from final surgery to chemotherapy (> 64 vs. ≤ 40 ; OR = 1.49; 95% CI = 1.04–2.14).

Conclusion Shorter wait times to most treatments for postmenopausal women diagnosed in BAC further supports that women with an abnormal mammogram should be managed through organized assessment. Continued evaluation of factors influencing wait times to treatment is essential for quality improvement and patient outcomes.

Résumé

Objectif On ignore si l'évaluation organisée de la santé du sein réduit les délais d'attente de traitement des femmes asymptomatiques. Le Programme ontarien de dépistage du cancer du sein (PODCS) offre le dépistage et l'évaluation organisée dans des centres d'évaluation de la santé du sein (CÉSS). Notre étude compare les délais d'attente selon la voie de traitement pour les femmes ayant subi un dépistage et reçu un diagnostic de cancer du sein dans des CÉSS ou par les soins habituels (SH).

Méthode Un protocole rétrospectif a permis de définir au sein du PODCS deux cohortes parallèles de femmes postménopausées âgées de 50 à 69 ans atteintes d'un cancer invasif du sein détecté par dépistage et évaluées dans des CÉSS ($n = 2\,010$) et par les SH ($n = 1\,844$) entre 2002 et 2010. Leurs caractéristiques démographiques ont été extraites du PODCS. Un résumé analytique des dossiers médicaux a fourni les données de pronostic et de traitement. Par régression logistique multinomiale, nous avons examiné les associations entre le type d'évaluation et les délais d'attente entre une mammographie anormale et la chirurgie, la chimiothérapie ou la radiothérapie.

✉ Anna M. Chiarelli
anna.chiarelli@cancercare.on.ca

Résultats Comparativement à celles ayant reçu un diagnostic par les soins habituels, les femmes postménopausées ayant reçu un diagnostic dans un centre d'évaluation de la santé du sein étaient significativement moins susceptibles d'avoir enduré des délais d'attente plus longs (en jours) entre une mammographie anormale et la chirurgie définitive (> 89 c. ≤ 47 ; RC = 0,63; IC de 95 % = 0,52–0,77), entre la dernière chirurgie et la radiothérapie (> 88 c. ≤ 55 ; RC = 0,71; IC de 95 % = 0,54–0,93) et entre la dernière chimiothérapie et la radiothérapie (> 41 c. ≤ 28 ; RC = 0,52; IC de 95 % = 0,36–0,76). À l'inverse, les femmes évaluées dans les CÉSS étaient plus susceptibles que celles évaluées par les soins habituels d'avoir enduré des délais d'attente plus longs entre la dernière chirurgie et la chimiothérapie (> 64 c. ≤ 40 ; RC = 1,49; IC de 95 % = 1,04–2,14).

Conclusion Les délais d'attente plus courts avant la plupart des traitements chez les femmes postménopausées ayant reçu un diagnostic dans un centre d'évaluation de la santé du sein constituent une preuve supplémentaire que les femmes ayant subi une mammographie anormale devraient être prises en charge par un programme d'évaluation organisé. Il est essentiel de poursuivre l'analyse des facteurs qui influent sur les délais d'attente de traitement pour améliorer la qualité des soins et l'issue pour les patientes.

Keywords Breast cancer · Organized breast assessment · Treatment wait times · Surgery · Chemotherapy · Radiotherapy

Mots-clés Cancer du sein · Évaluation organisée de la santé du sein · Délais d'attente de traitement · Chirurgie · Chimiothérapie · Radiothérapie

Introduction

The improved survival for women diagnosed with breast cancer has been attributed to a combination of early detection through mammography screening and advances in evidence-based treatment protocols (Canadian Cancer Society's Steering Committee. Canadian Cancer Statistics 2011). Despite improved survival outcomes, wait times across the breast cancer treatment pathway remain a concern. Studies have found that wait times greater than 12 weeks from an abnormal mammogram to definitive surgery are associated with decreased disease-free and cause-specific survival among women with early stage breast cancer (Vujovic et al. 2009). Delays of longer than 8 weeks (Huang et al. 2003) or delays of each additional month (Chen et al. 2008) to initiation of postoperative radiotherapy were associated with higher local recurrence rates, but not survival. However, a large Canadian study found that women waiting longer than 20 weeks for postoperative radiotherapy had higher recurrence rates and inferior breast-specific survival, compared with those who began within 4–8 weeks (Olivotto et al. 2009). Early initiation of postoperative chemotherapy improves overall survival for early stage breast cancer (Balduzzi et al. 2010). Similarly, a Canadian study found that women who received adjuvant chemotherapy earlier than 12 weeks after surgery had improved survival (Lohrisch et al. 2006). For radiotherapy postchemotherapy, risk of mortality was reduced when radiotherapy was given within 6 months of starting chemotherapy (Whelan et al. 2000).

Few studies have examined factors associated with variation in treatment wait times among asymptomatic women diagnosed with breast cancer. In Nova Scotia, Canada, women with stage I breast cancer experienced longer wait times from clinical or

mammographic detection to initiation of adjuvant therapy compared with those with more advanced disease (Rayson et al. 2004). Our previous study found that stage did not influence wait times to postoperative adjuvant therapy in either symptomatic or asymptomatic women (Plotogea et al. 2013). However, earlier stage was associated with shorter wait times from chemotherapy to radiotherapy among symptomatic women in another Ontario study (Benk et al. 2006). In two Canadian studies, including ours, wait times to postoperative adjuvant therapy were substantially longer for symptomatic women diagnosed more recently compared with those diagnosed earlier (Plotogea et al. 2013; Rayson et al. 2007). Similar delays for women diagnosed more recently were also observed in the United States among symptomatic women 65 or older for initiation of postoperative radiotherapy (Punglia et al. 2010).

The Ontario Breast Assessment Collaborative Group was established in 1998 to guide development of coordinated multidisciplinary approaches for facilities to provide organized breast assessment, resulting in the establishment of Breast Assessment Centres (BAC) (Ontario Breast Screening Program 2001). Our recent studies found that women assessed through BAC have shorter wait times to breast cancer diagnosis, and fewer, timelier, more appropriate assessment procedures compared with women seen through usual care (UC) (Chiarelli et al. 2017). Women with stage I screen-detected breast cancer assessed through BAC also have a reduced risk of all-cause mortality compared with those assessed through UC (Smith et al. 2018). Given these earlier findings and that BAC provide a more streamlined work-up and referral process for diagnosis, assessing the impact on subsequent breast cancer treatment wait times is important. To our knowledge, no studies to date have examined how organized breast assessment may influence treatment wait times among asymptomatic women.

This study compared wait times across phases of the breast cancer treatment pathway (from abnormal screen to definitive surgery, final surgery to chemotherapy or radiotherapy, final chemotherapy to radiotherapy) between concurrent cohorts of postmenopausal women aged 50–69 screened in the Ontario Breast Screening Program (OBSP) undergoing assessment through BAC and UC and diagnosed with invasive breast cancer. Comparisons in treatment wait times were also examined by stage and diagnosis period.

Methods

Study population

The study population has been previously described (Chiarelli et al. 2017; Smith et al. 2018). Briefly, the OBSP has been established since 1990 to provide a population-based breast screening program to eligible women (Chiarelli et al. 2013). Women are ineligible if they have a history of breast cancer, acute breast symptoms or current breast implants. Women aged 50–69 screened through the OBSP with an abnormal mammogram from January 1, 2002 to December 31, 2009 and diagnosed with breast cancer were identified. Although all women in the study were screened at an OBSP centre, assessment referral was dependent on whether the screening centre was affiliated with BAC. Women were followed prospectively to a definitive diagnosis. During the study period, women were screened at 150 OBSP centres and evaluated at 35 BAC.

Women with an abnormal mammogram underwent diagnostic assessment either through BAC or UC. Ontario facilities that provide organized assessment must meet established criteria to qualify as BAC. Criteria include: providing all abnormal mammographic work-up, including special mammographic views, ultrasound and image-guided core biopsy; providing radiological, surgical and pathologic consultation with experts in breast evaluation; and providing a navigator for patient support and referral coordination. BAC may either perform all the required services for abnormal mammographic work-up or establish networks with facilities to provide services (Quan et al. 2012). For women seen through UC, further diagnostic imaging after an abnormal mammogram is arranged directly from the screening centre and/or through their physician; results must be communicated to the physician, who is then responsible for arranging any further imaging or necessary biopsies and/or surgical consultation. Breast cancer treatment location is unrelated to where a woman had her breast assessment. The study was approved by the University of Toronto Research Ethics Board, and informed consent was not required.

Selection of breast cancer cases

To allow for learning curves for new BAC, only women with an abnormal mammogram assessed after 6 months of operation were selected (Jaro 1995). All postmenopausal women diagnosed with invasive breast cancers of any histological type detected within 12 months of an abnormal rescreen and classified as screen-detected by the program during follow-up were included. Women were excluded if they were premenopausal, a non-Ontario resident, treatment location was unknown, received treatment at a hospital with less than 15 eligible cases, or had bilateral or non-primary breast cancers that were detected on initial screens, diagnosed > 1 year after an abnormal screen or stage IV.

Data sources

Demographic and risk factor information were obtained from the Integrated Client Management System (ICMS) of the OBSP. Additional risk factor data, prognostic and treatment information were obtained from chart abstraction at regional cancer centres, which are specialized centres in Ontario that deliver all cancer radiotherapy; patients may also be referred for diagnostic work-up, systemic therapy and/or treatment planning. These centres maintain detailed patient charts about diagnostic and treatment information for care received at other institutions. A local collaborator was identified for each centre ($n = 13$) to facilitate chart abstraction and to obtain Research Ethics Board approval. Trained abstractors reviewed paper and electronic medical charts and used a standardized abstraction form to abstract relevant data.

Demographics and risk factors Diagnosis age and year were recorded. Women's postal code of residence at screening was linked to the 2006 Canadian Census to obtain income quintiles (Q1 (low)–Q5 (high)) and community status (Statistics Canada 2014). Community status was dichotomized into urban (population 10,000+) and non-urban, which included rural (< 10,000 and a strong metropolitan-influenced zone (MIZ)), rural remote (< 10,000 and a moderate MIZ) and rural very remote (< 10,000 and a weak/no MIZ) (Statistics Canada 2014).

Prognostic characteristics Stage was coded using the TNM classification scheme (6th ed.) (American Joint Committee on Cancer 2002). Estrogen, progesterone and HER2 protein receptors were coded as positive or negative; women who were negative for all three receptors were categorized as triple negative (Hammond et al. 2010; Wolff et al. 2007).

Wait times and treatment characteristics Date of abnormal screening mammogram prior to diagnosis for each woman was obtained through the ICMS. Treatment dates were abstracted from medical charts. Wait times (in days) were examined

across four phases in the treatment pathway: abnormal screening mammogram to definitive surgery (phase 1), final surgery to first chemotherapy (phase 2), final surgery to first radiotherapy without chemotherapy (phase 3) and final chemotherapy to first radiotherapy (phase 4). A definitive surgery was defined as the date of either partial mastectomy, modified radical mastectomy or total mastectomy and included surgeries occurring within 4 months of a tissue diagnosis. For women who underwent multiple surgeries ($n = 204$; 5.3% of cohort), the later surgery date was chosen as the date of definitive surgery. Final surgery was defined as the date of the last procedure before adjuvant treatment categorized as either partial mastectomy, modified radical mastectomy, total mastectomy, axillary node dissection or sentinel lymph node biopsy. Wait time to postoperative adjuvant treatment was calculated from the date of final surgery following diagnosis to the date of first adjuvant chemotherapy or radiotherapy. Adjuvant treatment included those occurring within 1 year of diagnosis. Receipt of adjuvant therapy for the primary diagnosis was dichotomized as 'yes' or 'no'. Hospital type where the woman had surgery was categorized as either 'academic' or 'community hospital'. Treatment centre region was grouped according to the regional cancer centre a woman first attended (South-Central, South-Eastern, South-Western and Northern) (Plotogea et al. 2013).

Statistical analysis

Demographic, prognostic and treatment characteristics were compared between BAC and UC using multivariable logistic regression to estimate adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs). For each treatment phase, wait times were summarized by the median, interquartile range (IQR) and ninetieth (90th) percentile. Comparisons of wait times between BAC and UC were performed using the Wilcoxon rank-sum tests (Haynes 2013). Wait times were categorized by quartiles calculated for all women for each treatment phase, with the first quartile as the referent group. Multinomial logistic regression examined associations between assessment type, stage and diagnosis period and wait times. Adjusted ORs and corresponding 95% CIs were estimated to quantify associations. Statistical tests were two-sided and evaluated at a 5% significance level. All analyses were performed using SAS version 9.4 (SAS Institute Inc 2013).

Results

Of the 155,866 women with an abnormal mammogram, 5260 (3.4%) were diagnosed with an invasive breast cancer on a rescreen (Fig. 1). After excluding $n = 1184$ women who did not meet our inclusion criteria, 4076 women were eligible for chart review. Among these women, 86 medical charts were unavailable, 18 were incomplete and 118 were ineligible after

chart review. The final sample consisted of 2010 postmenopausal women (52.2%) assessed through BAC and 1844 (47.8%) through UC. For treatment phases, 3699 women were included in the abnormal mammogram to definitive surgery phase 1 analysis, 1207 women in the final surgery to chemotherapy phase 2 analysis, 2012 women in the final surgery to radiotherapy phase 3 analysis, and 973 women in the final chemotherapy to radiotherapy phase 4 analysis.

Women assessed in BAC compared with UC were more likely to be diagnosed after 2006 than before (OR = 1.32; 95% CI 1.15–1.50), more likely to live in non-urban regions (OR = 1.23; 95% CI 1.04–1.46), more likely to have been seen at an academic centre for surgery (OR = 7.73; 95% CI 6.64–9.01), and more likely to have a total mastectomy as their definitive (OR = 1.78; 95% CI 1.33–2.40) and final surgery (OR = 1.46; 95% CI 1.15–1.86) (Table 1). Women assessed in BAC compared with UC were less likely to receive radiotherapy (OR = 0.79; 95% CI 0.67–0.93) and to receive treatment outside the South-Central region.

Among all women, the median wait time was 65 days (IQR = 47–89 days) from an abnormal mammogram to definitive surgery, 51 days (IQR = 40–64 days) from surgery to chemotherapy, 70 days (IQR = 55–88 days) from surgery to radiotherapy, and 33 days (IQR = 28–41 days) from chemotherapy to radiotherapy (Table 2). Median wait times were significantly shorter in BAC versus UC, except from final surgery to chemotherapy (54 vs. 49 days).

Women assessed through BAC compared with UC were less likely to experience longer wait times in the fourth compared with first quartile from an abnormal mammogram to definitive surgery (> 89 vs. ≤ 47 days; OR = 0.63) and from surgery to radiotherapy (> 88 vs. ≤ 55 days; OR = 0.71) (Table 3). Women evaluated in BAC were also less likely to experience longer wait times in the second (29–33 days; OR = 0.63), third (34–41 days; OR = 0.68) and fourth quartiles (> 41 days; OR = 0.52) compared with first (≤ 28 days) from chemotherapy to radiotherapy. Conversely, compared with UC, women assessed through BAC were more likely to experience longer wait times in the fourth compared with first quartile from surgery to chemotherapy (> 64 vs. ≤ 40 days; OR = 1.49).

Women diagnosed from 2006 to 2010 compared with from 2002 to 2005 were more likely to experience longer wait times in the second (48–65 days; OR = 1.26), third (66–89 days; OR = 1.67) and fourth quartiles (> 89 days; OR = 1.96) compared with first (≤ 47 days) from an abnormal mammogram to definitive surgery. However, they were less likely to experience longer wait times in the third (71–88 days; OR = 0.60) and fourth quartiles (> 88 days; OR = 0.48) compared with first from surgery to radiotherapy (Table 3).

Women with stage II/III compared with stage I breast cancers were less likely to have longer wait times in the second (48–65 days; OR = 0.80), third (66–89 days; OR = 0.74) and fourth quartiles (> 89 days; OR = 0.52) compared with first (≤ 47 days)

Fig. 1 Cohort of women aged 50–69 diagnosed with invasive breast cancer within the Ontario Breast Screening Program (OBSP) between January 1, 2002 and December 31, 2010 and included in the treatment pathway analysis according to Breast Assessment Centre (BAC) and usual care (UC)

from an abnormal mammogram to definitive surgery (Table 3). They were also less likely to have longer wait times in the fourth compared with first quartile from surgery to chemotherapy (> 64 vs. ≤ 40 days; OR = 0.55). Conversely, women with stage II/III breast cancer were more likely to experience longer wait times in the fourth compared with first quartile from final surgery to radiotherapy (> 88 vs. ≤ 55 days; OR = 2.48).

Discussion

To our knowledge, this study is the first to examine how organized breast assessment impacts treatment wait times in a population-based cohort of asymptomatic women with screen-detected invasive breast cancer. In Ontario,

postmenopausal women with an abnormal screening mammogram assessed through BAC experience reduced wait times to definitive surgery, from final surgery to radiotherapy, and from final chemotherapy to radiotherapy, but longer wait times from final surgery to chemotherapy.

An earlier study in Ontario found that delays longer than 12 weeks from an abnormal mammogram to definitive surgery were associated with decreased survival (Vujovic et al. 2009). In our cohort, 75% of women had their definitive surgery within 89 days (12.7 weeks) of their abnormal mammogram, and women evaluated in BAC compared with UC were significantly less likely to experience wait times longer than this. The reduced wait times to definitive surgery for women assessed through BAC might be explained by the multidisciplinary expertise, including surgical support, offered through these centres (Quan et al. 2012).

Table 1 Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for demographic characteristics, risk factors and prognostic characteristics among postmenopausal women diagnosed with screen-detected breast cancers through a Breast Assessment Centre versus through usual care

Characteristics	Breast assessment type			
	Usual care	Breast Assessment Centre	Overall	Adjusted OR ^a (95% CI)
	<i>N</i> = 1844 <i>n</i> (%)	<i>N</i> = 2010 <i>n</i> (%)	<i>N</i> = 3854 <i>n</i> (%)	
Demographic and risk factors				
Age at diagnosis (years)				
50–59	656 (35.6)	707 (35.2)	1363 (35.4)	1.00 (Ref.)
60–69	1188 (64.4)	1303 (64.8)	2491 (64.6)	1.01 (0.89–1.16)
Period of diagnosis				
2002–2005	692 (37.5)	630 (31.3)	1322 (34.3)	1.00 (Ref.)
2006–2010	1152 (62.5)	1380 (68.7)	2532 (65.7)	1.32 (1.15–1.50)
Community status				
Urban	1548 (84.0)	1630 (81.1)	3178 (82.5)	1.00 (Ref.)
Non-urban	294 (16.0)	380 (18.9)	674 (17.6)	1.23 (1.04–1.46)
Missing	2	0	2	
Income quintile				
1—Lowest	305 (16.7)	361 (18.1)	666 (17.4)	1.00 (Ref.)
2	347 (19.0)	396 (19.8)	743 (19.4)	0.96 (0.78–1.18)
3	360 (19.7)	403 (20.2)	763 (19.9)	0.94 (0.77–1.16)
4	365 (19.9)	385 (19.3)	750 (19.6)	0.89 (0.73–1.10)
5—Highest	454 (24.8)	455 (22.8)	909 (23.7)	0.85 (0.69–1.04)
Missing	13	10	23	
Prognostic factors				
Stage at diagnosis				
Stage I	1177 (65.4)	1299 (65.8)	2476 (65.6)	1.00 (Ref.)
Stage II/III	624 (34.6)	674 (34.2)	1298 (34.4)	0.97 (0.85–1.11)
Missing	43	37	80	
Triple negative				
No	1623 (91.5)	1761 (91.5)	3384 (91.5)	1.00 (Ref.)
Yes	150 (8.5)	164 (8.5)	314 (8.5)	0.99 (0.78–1.25)
Missing	71	85	156	
Treatment characteristics				
Hospital type				
Community hospital	1498 (81.8)	756 (38.0)	2254 (59.0)	1.00 (Ref.)
Academic centre	334 (18.2)	1231 (62.0)	1565 (41.0)	7.73 (6.64–9.01)
Missing	12	23	35	
Definitive surgery type ^b				
Partial mastectomy	1526 (83.1)	1590 (79.3)	3116 (81.2)	1.00 (Ref.)
Modified radical mastectomy	239 (13.0)	276 (13.8)	515 (13.4)	1.13 (0.94–1.36)
Total mastectomy	71 (3.9)	136 (6.8)	207 (5.4)	1.78 (1.33–2.40)
None	4	3	7	–
Missing	4	5	9	
Final surgery type ^{b,c}				
Partial mastectomy	1224 (66.7)	1283 (64.0)	2507 (65.3)	1.00 (Ref.)
Modified radical mastectomy	236 (12.8)	270 (13.4)	506 (13.1)	1.11 (0.92–1.35)
Total mastectomy	121 (6.6)	188 (9.4)	309 (8.0)	1.46 (1.15–1.86)
ALND/SLNB	255 (13.9)	265 (13.2)	520 (13.5)	1.00 (0.86–1.12)
Other	1	2	3	–

Table 1 (continued)

Characteristics	Breast assessment type			Adjusted OR ^a (95% CI)
	Usual care <i>N</i> = 1844 <i>n</i> (%)	Breast Assessment Centre <i>N</i> = 2010 <i>n</i> (%)	Overall <i>N</i> = 3854 <i>n</i> (%)	
None	3	2	5	—
Missing	4	0	4	
Chemotherapy				
No	1125 (61.8)	1231 (61.8)	2356 (61.8)	1.00 (Ref.)
Yes	696 (38.2)	761 (38.2)	1457 (38.2)	0.99 (0.87–1.13)
Missing	23	18	41	
Radiotherapy				
No	299 (16.3)	394 (19.7)	693 (18.1)	1.00 (Ref.)
Yes	1533 (83.7)	1610 (80.3)	3143 (81.9)	0.79 (0.67–0.93)
Missing	12	6	18	
Radiotherapy ^b				
No				
Partial mastectomy	92 (30.8)	100 (25.6)	192 (27.8)	1.00 (Ref.)
Modified radical mastectomy	151 (50.5)	180 (46.0)	331 (47.8)	1.12 (0.78–1.61)
Total mastectomy	53 (17.7)	109 (27.9)	162 (23.5)	1.85 (1.20–2.86)
Yes				
Partial mastectomy	1424 (93.1)	1487 (92.5)	2911 (92.8)	1.00 (Ref.)
Modified radical mastectomy	87 (5.7)	94 (5.9)	181 (5.8)	1.03 (0.76–1.39)
Total mastectomy	17 (1.1)	26 (1.6)	43 (1.4)	1.37 (0.74–2.54)
Treatment centre region				
South-Central	1131 (61.3)	727 (36.2)	1858 (48.2)	1.00 (Ref.)
South-Eastern	170 (9.2)	548 (27.3)	718 (18.6)	5.32 (4.36–6.49)
South-Western	289 (15.7)	457 (22.7)	746 (19.4)	2.52 (2.11–3.00)
Northern	254 (13.8)	278 (13.8)	532 (13.8)	1.78 (1.47–2.17)

^a Adjusted by age at diagnosis and/or period of diagnosis

^b Partial mastectomy = partial mastectomy with or without axillary node dissection or sentinel lymph node biopsy on the same day; modified radical mastectomy = modified radical mastectomy with or without sentinel lymph node biopsy on the same day or total mastectomy with axillary node dissection on the same day; total mastectomy = total mastectomy with sentinel lymph node biopsy on the same day

^c Axillary lymph node dissection (ALND)/sentinel lymph node biopsy (SLNB) performed on separate day from other procedures

Our median wait time of 70 days (10.0 weeks) from surgery to radiotherapy is within those recommended by the Canadian Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer (Whelan et al. 2003) and falls within the range of median wait times (63–84 days) reported in earlier Canadian studies (Olivotto et al. 2009; Benk et al. 2006). Women assessed in BAC were also significantly less likely to experience wait times longer than 88 days (12.6 weeks) to postoperative radiotherapy compared with women assessed through UC. An earlier Canadian study found that 23% of patients had intervals greater than 12 weeks from surgery to radiotherapy (Olivotto et al. 2009), compared with 22% in BAC and 28% in UC. In Canada, delays of longer than 20 weeks to postoperative radiotherapy, compared with 4–8 weeks, have been associated with higher recurrence rates and inferior breast-specific survival (Olivotto et al. 2009).

Median wait time from final surgery to chemotherapy was 51 days in our cohort, longer than the 43 days reported in our earlier study of Ontario women with screen-detected breast cancer (Plotogea et al. 2013). Longer wait times to chemotherapy in the current study may represent a temporal effect due to increased use of chemotherapy for node-negative breast cancer in recent years (Plotogea et al. 2013). Contrary to our findings for definitive surgery and postoperative radiotherapy, women assessed in BAC were significantly more likely to experience longer wait times to postoperative chemotherapy compared with women assessed in UC. This may be explained by our finding that more women assessed in BAC had total mastectomy as their final surgery and longer postoperative recovery could have delayed treatment initiation (Saint-Jacques et al. 2007). In addition, women assessed in BAC were more likely to have surgery at an academic centre and

Table 2 Median wait times (in days), interquartile range and 90th percentile to definitive surgery, chemotherapy, and radiotherapy overall, and among postmenopausal women diagnosed with screen-detected breast cancers through a Breast Assessment Centre versus through usual care

	Overall <i>N</i> = 3854 <i>n</i> (%)	Usual care <i>N</i> = 1844 <i>n</i> (%)	Breast Assessment Centre <i>N</i> = 2010 <i>n</i> (%)
Treatments received ^a			
Surgery + chemotherapy	242 (6.4)	102 (5.6)	140 (7.0)
Surgery + radiotherapy	1907 (50.3)	931 (51.6)	976 (49.1)
Surgery + chemotherapy + radiotherapy	1203 (31.7)	583 (32.3)	620 (31.2)
Surgery only	441 (11.6)	190 (10.5)	251 (12.6)
Missing	61	38	23
Abnormal screen to definitive surgery ^b			
Number in analysis	3699	1775	1924
Median wait time to definitive surgery	65	67	63
Interquartile range	47–89	47–91	47–85
> 90th Percentile	117	123	112
Final surgery to chemotherapy ^c			
Number in analysis	1207	544	663
Median wait time to chemotherapy	51	49	54
Interquartile range	40–64	37–62	42–65
> 90th percentile	76	74	77
Final surgery to radiotherapy ^d			
Number in analysis	2012	1001	1011
Median wait time to radiotherapy	70	71	69
Interquartile range	55–88	55–91	55–84
> 90th percentile	114	125	107
Final chemotherapy to radiotherapy ^e			
Number in analysis	973	449	524
Median wait time to radiotherapy	33	33	32
Interquartile range	28–41	28–41	27–40
> 90th percentile	55	56	53

^a Pearson chi-squared test; difference in treatments received for BAC compared with UC ($p = 0.0463$)

^b Wilcoxon rank sum test; difference in wait times for BAC compared with UC ($p = 0.0289$)

^c Wilcoxon rank sum test; difference in wait times for BAC compared with UC ($p < 0.0001$)

^d Wilcoxon rank sum test; difference in wait times for BAC compared with UC ($p = 0.0028$)

^e Wilcoxon rank sum test; difference in wait times for BAC compared with UC ($p = 0.0068$)

possibly more likely to be referred for further testing prior to chemotherapy initiation. An earlier Canadian study found that delays longer than 12 weeks to postoperative chemotherapy were associated with inferior survival (Lohrisch et al. 2006).

Another Canadian study has examined wait times from final chemotherapy to radiotherapy in symptomatic women and found a median wait time of 5.3 weeks, slightly longer than ours of 33 days (4.7 weeks) (Benk et al. 2006). Organized breast assessment had the greatest impact on wait times along this phase of the treatment pathway, with women evaluated in BAC significantly less likely to experience wait times longer than 28 days (4 weeks) compared with those evaluated in UC. This finding is unexpected since this treatment phase occurs furthest temporally from diagnostic assessment and completely within the cancer system and should be least impacted by diagnosis through BAC.

In our cohort, diagnosis period was associated with wait times from an abnormal mammogram to definitive surgery and to postoperative radiotherapy. More than half of women (53%) diagnosed with breast cancer from 2006 to 2010 waited longer than 65 days from an abnormal mammogram to surgery, compared with 42% of women diagnosed from 2002 to 2005. Longer wait times to definitive surgery may be due to the increase in breast cancer incidence (Canadian Cancer Society's Steering Committee. Canadian Cancer Statistics 2011) and more complex imaging work-up and surgeries over time. Contrary to earlier studies (Rayson et al. 2007; Punglia et al. 2010), we found that wait times to postoperative radiotherapy were shorter for our more recent time period compared with the earlier one. A possible explanation for this discrepancy might be that earlier studies included mostly symptomatic women, and the US study only

Table 3 Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) describing factors associated with wait times (in days) from abnormal screen to definitive surgery, from final surgery to postoperative chemotherapy or postoperative radiotherapy and from final chemotherapy to radiotherapy

	Breast assessment type			Period of diagnosis			Stage		
	Usual care <i>N</i> (%)	BAC <i>N</i> (%)	Adjusted OR (95% CI)	2002–2005 <i>N</i> (%)	2006–2010 <i>N</i> (%)	Adjusted OR (95% CI)	I <i>N</i> (%)	II/III <i>N</i> (%)	Adjusted OR (95% CI)
Abnormal screen to definitive surgery ^a (<i>n</i> = 3699)									
≤ 47 days	456 (25.7)	498 (25.9)	1.00 (Ref.)	395 (31.1)	559 (23.0)	1.00 (Ref.)	568 (23.4)	372 (30.7)	1.00 (Ref.)
48 to 65 days	405 (22.8)	525 (27.3)	1.05 (0.86–1.27)	337 (26.6)	593 (24.4)	1.26 (1.04–1.53)	600 (24.7)	316 (26.1)	0.80 (0.66–0.97)
66 to 89 days	436 (24.6)	472 (24.5)	0.85 (0.70–1.03)	275 (21.7)	633 (26.1)	1.67 (1.37–2.04)	598 (24.7)	293 (24.2)	0.74 (0.60–0.89)
> 89 days	478 (26.9)	429 (22.3)	0.63 (0.52–0.77)	262 (20.7)	645 (26.5)	1.96 (1.60–2.39)	660 (27.2)	231 (19.1)	0.52 (0.42–0.64)
Final surgery to first chemotherapy ^b (<i>n</i> = 1207)									
≤ 40 days	165 (30.3)	140 (21.1)	1.00 (Ref.)	97 (25.4)	208 (25.2)	1.00 (Ref.)	82 (20.6)	222 (27.5)	1.00 (Ref.)
41 to 51 days	145 (26.7)	165 (24.9)	1.26 (0.90–1.78)	101 (26.4)	209 (25.3)	0.88 (0.61–1.27)	101 (25.4)	209 (25.9)	0.84 (0.57–1.23)
52 to 64 days	125 (23.0)	186 (28.1)	1.39 (0.98–1.96)	93 (24.4)	218 (26.4)	1.12 (0.77–1.62)	100 (25.1)	210 (26.0)	0.82 (0.55–1.21)
> 64 days	109 (20.0)	172 (25.9)	1.49 (1.04–2.14)	91 (23.8)	190 (23.0)	0.92 (0.63–1.34)	115 (28.9)	166 (20.6)	0.55 (0.37–0.81)
Final surgery to first radiotherapy ^c (<i>n</i> = 2012)									
≤ 55 days	261 (26.1)	279 (27.6)	1.00 (Ref.)	147 (21.0)	393 (30.0)	1.00 (Ref.)	467 (28.0)	63 (21.0)	1.00 (Ref.)
56 to 70 days	225 (22.5)	276 (27.3)	1.12 (0.86–1.46)	148 (21.1)	353 (26.9)	0.92 (0.69–1.22)	437 (26.2)	54 (18.0)	0.92 (0.62–1.36)
71 to 88 days	233 (23.3)	239 (23.6)	0.89 (0.68–1.16)	184 (26.3)	288 (22.0)	0.60 (0.45–0.80)	409 (24.5)	56 (18.7)	1.02 (0.69–1.52)
> 88 days	282 (28.2)	217 (21.5)	0.71 (0.54–0.93)	222 (31.7)	277 (21.1)	0.48 (0.36–0.63)	354 (21.2)	127 (42.3)	2.48 (1.74–3.53)
Final chemotherapy to first radiotherapy ^d (<i>n</i> = 973)									
≤ 28 days	127 (28.3)	198 (37.8)	1.00 (Ref.)	94 (30.8)	231 (34.6)	1.00 (Ref.)	102 (32.9)	223 (33.7)	1.00 (Ref.)
29 to 33 days	110 (24.5)	106 (20.2)	0.63 (0.44–0.92)	58 (19.0)	158 (23.7)	1.19 (0.80–1.76)	69 (22.3)	147 (22.2)	0.99 (0.68–1.44)
34 to 41 days	101 (22.5)	105 (20.0)	0.68 (0.47–0.98)	69 (22.6)	137 (20.5)	0.86 (0.58–1.26)	63 (20.3)	143 (21.6)	1.03 (0.71–1.51)
> 41 days	111 (24.7)	115 (22.0)	0.52 (0.36–0.76)	84 (27.5)	142 (21.3)	0.79 (0.53–1.15)	76 (24.5)	149 (22.5)	0.90 (0.62–1.31)

BAC Breast Assessment Centre

^a Adjusted for assessment pathway, age, period of diagnosis, treatment centre region, stage and definitive surgery type^b Adjusted for assessment pathway, age, period of diagnosis, treatment centre region, stage, final surgery type and triple negative status^c Adjusted for assessment pathway, age, period of diagnosis, treatment centre region, stage and final surgery type^d Adjusted for assessment pathway, age, period of diagnosis, treatment centre region and stage

considered women aged 65 or older (Punglia et al. 2010). Since 2004, Cancer Care Ontario has been publicly reporting wait times to radiotherapy (Cancer Care Ontario 2010), and improved wait times from 2006 to 2010 might be attributable to better planning and new investments in regional cancer centres, radiation equipment and personnel initiated in the early 2000s. The shorter wait times to postoperative radiotherapy in BAC may be explained by our finding that women assessed in BAC were more likely to be diagnosed from 2006 to 2010, when wait times to radiotherapy were shorter.

The effect of stage on wait time from abnormal mammogram to definitive surgery has not been previously examined. In our cohort, women with stage II/III compared with stage I breast cancers were significantly less likely to wait longer than 47 days (6.7 weeks) for their definitive surgery. Contrary to our earlier Ontario study (Plotgea et al. 2013), stage also impacted wait times to postoperative chemotherapy, with significantly fewer women with stage II/III breast cancers having longer wait times (> 64 days or 9.1 weeks). Our observation of

shorter wait times to definitive surgery and chemotherapy for higher stage cancers is consistent with the expedition of treatment of more severe cases observed in other Canadian provinces (Caplan et al. 2000). Unexpectedly, we found that women diagnosed with stage II/III breast cancer were more likely to experience wait times longer than 88 days (12.6 weeks) from surgery to radiotherapy. Although these women did not receive chemotherapy, they likely would have been referred for consideration of systemic therapy; the increased wait time to postoperative radiotherapy likely includes time for medical oncology consultation and further testing.

Strengths of this study include its use of data from a large population-based cohort of screened women with invasive breast cancer. Selection bias was limited, as women were assessed through BAC or UC by the affiliation of their OBSP screening site. We were also able to obtain detailed information on treatment dates and types through chart abstraction. There were also some limitations. Our results may not be generalizable to symptomatic or opportunistically screened women; however in

Ontario, the majority of women aged 50–69 undergo breast cancer screening within the OBSP (Cancer Care Ontario 2016). The inclusion of premenopausal women and those with bilateral breast cancer may have also provided more generalizable results; however, there were very few in our cohort. As only rescreeens (incident breast cancers) were included, treatment wait times may not apply to prevalent cancers. Although we measured and adjusted for differences in patient populations (i.e., period of diagnosis, treatment centre region), cohort designs are limited by non-randomization of exposure and adjustment may not have fully addressed these potential confounders. Additionally, patient and system-level factors that can influence wait times, such as patient beliefs and attitudes, logistical barriers to accessing treatment, delays in treatment seeking, appointment scheduling or availability of physicians, were not captured by our data.

Conclusion

Delays to breast cancer treatment are associated with increased risk of recurrence and reduced survival. Assessing factors influencing wait times along the breast cancer treatment pathway is important to identify areas for quality improvement, with the ultimate goal of improving patient outcomes. This study examined the impact of organized breast assessment on treatment wait times in a large cohort of asymptomatic postmenopausal women. With the exception of time to postoperative chemotherapy, women in BAC experienced shorter wait times to definitive surgery, postoperative radiotherapy and from chemotherapy to radiotherapy compared with women in UC. These results and those of our earlier studies (Chiarelli et al. 2017; Smith et al. 2018) further support that women with an abnormal mammogram should be managed through organized assessment.

Acknowledgements We thank the study staff, Brittany Speller, Leanne Lindsay, Lucy Leon and Anjali Pandya. We also thank Jessie Cunningham for assisting in the literature search. We acknowledge Cancer Care Ontario for use of its data.

Funding information This work was supported by the Canadian Institutes of Health Research (grant number 130400). This agency had no involvement in the study design, data collection, analysis, interpretation, manuscript preparation or the decision to submit the manuscript for publication.

Compliance with ethical standards

We can confirm that we have observed appropriate ethical guidelines and legislation in conducting the study. The study was approved by the University of Toronto Research Ethics Board (Protocol #29342), and informed consent was not required as there was no direct contact with women and the study falls within the ethical domain of non-consensual research. In addition, Research Ethics Board approval was obtained for each regional cancer centre for medical chart abstraction.

Conflict of interest The authors declare that they have no conflict of interest.

References

- American Joint Committee on Cancer. (2002). *Cancer staging manual* (6th ed.). New York: Springer-Verlag.
- Balduzzi, A., Leonardi, M. C., Cardillo, A., Orecchia, R., Dellapasqua, S., Iorfida, M., et al. (2010). Timing of adjuvant systemic therapy and radiotherapy after breast-conserving surgery and mastectomy. *Cancer Treatment Reviews*, 36(6), 443–450 **Epub 2010 Mar 20**.
- Benk, V., Przybysz, R., McGowan, T., & Paszat, L. (2006). Waiting times for radiation therapy in Ontario. *Canadian Journal of Surgery*, 49(1), 16–21.
- Canadian Cancer Society's Steering Committee. Canadian Cancer Statistics. (2011). *Toronto* (p. 2011). ON: Canadian Cancer Society.
- Cancer Care Ontario. (2010). *Wait Times*. from: <http://www.cancercare.on.ca/cms/One.aspx?portalId=1377&pageId=8836>. Accessed 04/29/2013, 2013.
- Cancer Care Ontario. (2016). *Ontario Cancer Screening Performance Report 2016*. Toronto.
- Caplan, L. S., May, D. S., & Richardson, L. C. (2000). Time to diagnosis and treatment of breast cancer: Results from the National Breast and Cervical Cancer Early Detection Program, 1991–1995. *American Journal of Public Health*, 90(1), 130–134.
- Chen, Z., King, W., Pearcey, R., Kerba, M., & Mackillop, W. J. (2008). The relationship between waiting time for radiotherapy and clinical outcomes: a systematic review of the literature. *Radiotherapy and Oncology*, 87(1), 3–16 **Epub 2007 Dec 21**.
- Chiarelli, A. M., Edwards, S. A., Prummel, M. V., Muradali, D., Majpruz, V., Done, S. J., et al. (2013). Digital compared with screen-film mammography: performance measures in concurrent cohorts within an organized breast screening program. *Radiology*, 268(3), 684–693.
- Chiarelli, A. M., Muradali, D., Blackmore, K. M., Smith, C. R., Mirea, L., Majpruz, V., et al. (2017). Evaluating wait times from screening to breast cancer diagnosis among women undergoing organised assessment vs usual care. *British Journal of Cancer*, 116(10), 1254.
- Hammond, M. E., Hayes, D. F., Dowsett, M., Allred, D. C., Hagerty, K. L., Badve, S., et al. (2010). American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer (unabridged version). *Archives of Pathology & Laboratory Medicine*, 134(7), e48–e72.
- Haynes, W. (2013). Wilcoxon rank sum test. In *Encyclopedia of Systems Biology* (pp. 2354–2355). Berlin: Springer.
- Huang, J., Barbera, L., Brouwers, M., Browman, G., & Mackillop, W. J. (2003). Does delay in starting treatment affect the outcomes of radiotherapy? A systematic review. *Journal of Clinical Oncology*, 21(3), 555–563.
- Jaro, M. A. (1995). Probabilistic linkage of large public health data files. *Statistics in Medicine*, 14(5–7), 491–498.
- Lohrisch, C., Paltiel, C., Gelmon, K., Speers, C., Taylor, S., Barnett, J., et al. (2006). Impact on survival of time from definitive surgery to initiation of adjuvant chemotherapy for early-stage breast cancer. *Journal of Clinical Oncology*, 24(30), 4888–4894 **Epub 2006 Oct 2**.
- Olivetto, I. A., Lesperance, M. L., Truong, P. T., Nichol, A., Berrang, T., Tyldesley, S., et al. (2009). Intervals longer than 20 weeks from breast-conserving surgery to radiation therapy are associated with inferior outcome for women with early-stage breast cancer who are not receiving chemotherapy. *Journal of Clinical Oncology*, 27(1), 16–23 **Epub 2008 Nov 17**.
- Ontario Breast Screening Program. (2001). *Multidisciplinary Roles and Expectations for Breast Assessment in Ontario*. Toronto: The Breast Assessment Collaborative Group.
- Plotogea, A., Chiarelli, A. M., Mirea, L., Prummel, M. V., Chong, N., Shumak, R. S., et al. (2013). Factors associated with wait times across the breast cancer treatment pathway in Ontario. *SpringerPlus*, 2(1), 388. <https://doi.org/10.1186/2193-1801-2-388>.

- Punglia, R. S., Saito, A. M., Neville, B. A., Earle, C. C., & Weeks, J. C. (2010). Impact of interval from breast conserving surgery to radiotherapy on local recurrence in older women with breast cancer: retrospective cohort analysis. *Bmj*, 340, c845.
- Quan, M. L., Shumak, R. S., Majpruz, V., Holloway, C. M., O'Malley, F. P., & Chiarelli, A. M. (2012). Improving work-up of the abnormal mammogram through organized assessment: results from the ontario breast screening program. *Journal of Oncology Practice/ American Society of Clinical Oncology*, 8(2), 107–112.
- Rayson, D., Chiasson, D., & Dewar, R. (2004). Elapsed time from breast cancer detection to first adjuvant therapy in a Canadian province, 1999–2000. *CMAJ*, 170(6), 957–961.
- Rayson, D., Saint-Jacques, N., Younis, T., Meadows, J., & Dewar, R. (2007). Comparison of elapsed times from breast cancer detection to first adjuvant therapy in Nova Scotia in 1999/2000 and 2003/04. *CMAJ*, 176(3), 327–332.
- Saint-Jacques, N., Younis, T., Dewar, R., & Rayson, D. (2007 12/1906/30/received 11/10/13/accepted). Wait times for breast cancer care. *British Journal of Cancer*, 96(1), 162–168.
- SAS Institute Inc. (2013). *Statistical Analysis Software, 9.4 ed.* Cary: SAS Institute.
- Smith, C. R., Chiarelli, A. M., Holloway, C. M., Mirea, L., O'Malley, F. P., Blackmore, K. M., et al. (2018). The impact of organized breast assessment on survival by stage for screened women diagnosed with invasive breast cancer. *The Breast*, 41, 25–33.
- Statistics Canada. Postal code conversion file plus (PCCF+), reference guide, 2014.
- Vujovic, O., Yu, E., Cherian, A., Perera, F., Dar, A. R., Stitt, L., et al. (2009). Effect of interval to definitive breast surgery on clinical presentation and survival in early-stage invasive breast cancer. *International Journal of Radiation Oncology, Biology, Physics*, 75(3), 771–774.
- Whelan, T. J., Julian, J., Wright, J., Jadad, A. R., & Levine, M. L. (2000). Does locoregional radiation therapy improve survival in breast cancer? A meta-analysis. *Journal of Clinical Oncology*, 18(6), 1220–1229 e-pub ahead of print 2000/03/15.
- Whelan, T., Olivetto, I., & Levine, M. (2003). Health Canada's Steering Committee on Clinical Practice Guidelines for the C, Treatment of Breast C. Clinical practice guidelines for the care and treatment of breast cancer: breast radiotherapy after breast-conserving surgery (summary of the 2003 update). *CMAJ*, 168(4), 437–439.
- Wolff, A. C., Hammond, M. E., Schwartz, J. N., Hagerty, K. L., Allred, D. C., Cote, R. J., et al. (2007). American Society of Clinical Oncology/ College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *Archives of Pathology & Laboratory Medicine*, 131(1), 18–43.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Affiliations

Kristina M. Blackmore¹ · Ashini Weerasinghe¹ · Claire M. B. Holloway^{2,3} · Vicky Majpruz¹ · Lucia Mirea^{4,5} · Frances P. O'Malley⁶ · Cathy Paroschy Harris⁷ · Ashley Hendry⁸ · Amanda Hey⁹ · Anat Kornecki¹⁰ · George Lougheed¹¹ · Barbara-Anne Maier¹² · Patricia Marchand¹³ · David McCready^{3,14} · Carol Rand¹⁵ · Simon Raphael¹⁶ · Roanne Segal-Nadler¹⁷ · Neelu Sehgal¹⁸ · Derek Muradali^{1,19,20} · Anna M. Chiarelli^{1,5}

¹ Prevention and Cancer Control, Cancer Care Ontario, 620 University Avenue, Toronto, Ontario M5G 2L7, Canada

² Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada

³ Department of Surgery, University of Toronto, 149 College Street, 5th Floor, Toronto, Ontario M5T 1P5, Canada

⁴ Phoenix Children's Hospital, 1919 East Thomas Road, Phoenix, AZ 85016, USA

⁵ Dalla Lana School of Public Health, University of Toronto, 155 College Street, 6th floor, Toronto, Ontario M5T 3M7, Canada

⁶ Department of Laboratory Medicine, St. Michael's Hospital, 30 Bond Street, Toronto, Ontario M5B 1W8, Canada

⁷ Prevention and Screening Services, Thunder Bay Regional Health Sciences Centre, 980 Oliver Road, Thunder Bay, Ontario P7B 6V4, Canada

⁸ South East Regional Cancer Program, 25 King Street, West Kingston, Ontario K7L 5P9, Canada

⁹ North East Regional Cancer Program, 41 Ramsey Lake Road, Sudbury, ON P3E 5J1, Canada

¹⁰ South West Regional Cancer Program, 790 Commissioners Road, East London, Ontario N6A 4L6, Canada

¹¹ North Simcoe Muskoka Regional Cancer Program, 201 Georgian Drive, Barrie, ON L4M 6M2, Canada

¹² Waterloo Wellington Regional Cancer Program, 835 King Street, West Kitchener, Ontario N2G 1G3, Canada

¹³ Central East Regional Cancer Program, 1 Hospital Court, Oshawa, Ontario L1G 2B9, Canada

¹⁴ Princess Margaret Cancer Centre, 610 University Ave, Toronto, Ontario M5G 2M9, Canada

¹⁵ Hamilton Niagara Haldimand Brant Regional Cancer Program, 699 Concession Street, Hamilton, Ontario L8V 5C2, Canada

¹⁶ North York General Hospital, 4001 Leslie St., North York, Ontario M2K 1E1, Canada

¹⁷ Champlain Regional Cancer Program, 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada

¹⁸ Erie St. Clair Regional Cancer Program, 2220 Kildare Road, Windsor, Ontario N8W 2X3, Canada

¹⁹ St. Michael's Hospital, 30 Bond Street, Toronto, Ontario M5B 1W8, Canada

²⁰ Department of Medical Imaging, University of Toronto, 263 McCaul Street, 4th Floor, Toronto, Ontario M5T 1W7, Canada