

Will COVID-19 directives to reduce regularly scheduled physical examinations affect recurrence detection in early breast cancer patients?

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Abstract

Purpose: The COVID-19 pandemic resulted in a rapid move to virtual care. Questions exist as to whether reduced in-person assessment, with physical examination of early breast cancer patients (EBC), will affect the detection of recurrences. We evaluated recurrence patterns of patients transferred into a survivorship program through a single centre Wellness Beyond Cancer Program (WBCP).

Methods: Consecutive EBC patients who returned to formal oncologist follow-up between February 1, 2013, and January 1, 2019, due to breast cancer recurrence were reviewed. Descriptive analyses were used to present patients and disease characteristics stratified by type of recurrence and mode of cancer detection.

Results: Of 206 recurrences, 41 were ipsilateral breast recurrences (19.9%), 135 were distant recurrences (65.5%), and 30 were contralateral new breast cancers (14.6%). Ipsilateral breast recurrences were detected by patients in 53.7% (22/41) of cases and by routine imaging in 41.5% (17/21). The majority of distant recurrences (125/135, 92.6%) were detected via patient-reported symptoms. Contralateral breast primaries were primarily detected by imaging 83.3% (25/30) and patient-reported symptoms 16.7%, (5/30). Only 2/206 (1.14%) recurrences/new primaries were detected by healthcare providers at routinely scheduled follow-up visits.

Conclusions: Despite following ASCO follow-up guidelines, healthcare providers rarely detect recurrences at routine follow-up appointments. While reduced in-person visits may affect other aspects of follow-up care (e.g. toxicity management), it appears unlikely, provided patients attend regular screening tests, that less frequent in-person follow-up is associated with worse breast cancer-related outcomes.

Introduction

The COVID-19 pandemic rapidly changed routine “well follow-up” care of patients with early breast cancer (EBC) who have completed the acute phase of their treatment (i.e. surgery/radiation and/or chemotherapy). Instead of routine, regularly scheduled, in-person follow-up with their healthcare provider, care has become primarily virtual with many patients having no routine physical examinations. Traditionally, the goals of such healthcare provider follow-up include; early detection of recurrence, evaluation and treatment of therapy-related complications, motivation of patients to continue therapy, and provision of ongoing support [1]. However, the quality of evidence around whether or not standardized follow-up is achieving these goals remains conflicting [2, 3]. Given the rapid change in the type of follow-up care provided as a result of COVID-19 mandates, this is a unique opportunity for patients and healthcare providers to review the goals of such follow-up.

The Ottawa Hospital Cancer Centre created a survivorship program, the Wellness Beyond Cancer Program (WBCP), in 2012. Patients are divided into two streams; either referred back to their primary care provider (PCP) or for patients with more complex care needs to a nurse practitioner within the cancer centre. The recommendations for follow-up in both these streams are based on ASCO/CCO recommendations [4, 5].

These guidelines recommend regularly scheduled physical examination every 3 to 6 months for the first 3 years after the completion of primary therapy, then every 6 to 12 months for years 4 and 5, then annually. If a patient within the WBCP develops signs or symptoms suggestive of recurrence, they have expedited re-entry into the cancer center for evaluation.

Given that we do not yet have data of how fewer scheduled in-person visits with physical examination has impacted recurrence detection, we reviewed the recurrence patterns from our WBCP patient population before the COVID-19 pandemic when they underwent routinely scheduled follow-up visits and physical exams. This provides an important opportunity to review the outcomes of a program that follows ASCO follow-up guidelines and analyze the patient population, looking at both patient and tumour characteristics of recurrence. The results of the current analysis would be to evaluate whether standard follow-up is effective for recurrence detection and, if not, to explore whether new, risk-based strategies may be more appropriate when the current pandemic ends.

Materials And Methods

Wellness Beyond Cancer Program (WBCP)

The Ottawa Cancer Program is a large cancer centre providing care for a population of approximately 1.5 million patients across Eastern Ontario[4]. After completion of the acute phase of cancer treatment, most patients are either referred back to their PCP with an individualized care plan; or transitioned to a nurse practitioner within the cancer centre for follow-up[4]. Some patients, though referred back to their PCP or NP, still have ongoing follow-up with their radiation oncologist or breast surgeon. The choice of which stream patients are referred to, and when the referral is made, is based on the ongoing risk of recurrence (based on physician evaluation), patient complexity and whether they have ongoing systemic therapies such as adjuvant bisphosphonates. Patients can be referred back to their original treating oncology team at the cancer center for recurrence, toxicity management or endocrine therapy duration re-assessment (Fig. 1).

Study Population

A retrospective chart review was conducted of both male and female breast cancer patients who entered the WBCP and were subsequently referred back to their oncologist (surgical, medical or radiation) during a six-year period from the conception of the program (February 1, 2013) to January 1, 2019, for a first breast cancer recurrence or a new contralateral primary (Fig. 1). These timelines were selected to allow a sufficient number of patients to enter the program and have at least one regularly planned visit to their healthcare provider and the start of the COVID-19 pandemic (March 2020).

Patients were excluded if they had a second recurrence, if they recurred prior to their initial assessment by the WBCP, or if the recurrence occurred after the end of January 2019. We reviewed patient baseline characteristics at the time of EBC diagnosis, including age, mode of primary cancer detection (screen vs self-detected), histologic subtype, tumour size, nodal status, estrogen-receptor (ER), progesterone-receptor

(PR) and human epidermal growth factor receptor 2 (HER2) status, date and type of surgery (mastectomy/lumpectomy), type(s) of treatment received (chemotherapy, hormonal therapy, anti-HER2 treatment, bisphosphonates, radiation treatment).

Study Outcomes

For those patients referred back to their oncologist with a documented recurrence, we evaluated outcomes including the type of recurrence (ipsilateral breast recurrence or distant recurrence) or new contralateral breast cancer. We also evaluated how the recurrence was detected (patient-reported symptoms, imaging-detected or health-care provider detected), and the most common patient-reported symptoms and location of recurrence. Local recurrence was defined as a biopsy positive for carcinoma in situ or invasive breast cancer in the ipsilateral breast and/or regional lymph nodes.

Data analysis

Descriptive statistics were used to summarize patients' baseline characteristics, treatment characteristics and outcomes. Categorical variables were presented in frequency and compared by Chi-squared tests. Continuous variables were presented in means and compared by Wilcoxon rank sum tests.

Results

The Wellness Program Referrals

Referral of breast cancer patients commenced February 2013, and as of January 2019, 5,472 patients had been transitioned through this program; 3,859 to their PCP and 1,615 to the NP (Supplemental Table 1).

Reasons for re-referral

We reviewed a total of 544 charts of patients who were referred back to their oncologist between February 1, 2013, and January 1, 2019. Of the 544 patients reviewed, 245 of these referrals were for breast cancer recurrence/new contralateral primaries. The remaining 299 were referred back for radiation oncology assessment or hormonal treatment re-assessment (i.e., assessing whether the patient should continue on their current hormonal therapy or switch to an alternate therapy and what duration they should continue for). Of the 245 patients with recurrences, 39 were excluded for: recurrence prior to WBCP referral (19), recurrence prior to first wellness assessment (8), a previous history of breast cancer recurrence (4), patients treated at another centre (2), and recurrence that occurred after January 1, 2019 (6) (Fig. 2). Baseline characteristics of the 206 eligible patients included in this analysis are included in Table 1. The information on patient demographics, tumour characteristics and details on recurrence were obtained (Table 2).

Table 1
Baseline characteristics of recurrences (n, 206)

		ALL PATIENTS (n = 206)
Age	Mean (sd)	59.0 (12.3)
	Median (range)	59 (25–90)
Mode of presentation for initial cancer	N (%) Self-detected	136 (66.0)
	Screen	63 (30.6)
	NA	7 (3.4)
Cancer		
Histology	Ductal	167 (81.1)
	Lobular	29 (14.1)
	Mixed	6 (2.9)
	DCIS	3 (1.5)
	Other	1 (0.5)
Grade	1	28 (14.2)
	2	80 (40.6)
	3	89 (45.2)
	NA	9
N Stage	0	87 (42.2)
	1	72 (35.0)
	2	26 (12.6)
	3	16 (7.8)
	NX	5 (2.4)
Size (cm)	Median (range)	2.5 (0, 14)
	NA	9
ER	N (%) Positive	165 (80.1)
PR	N (%) Positive	146 (70.9)

‡ abdominal pain or abdominal distension

* Patients with unknown Her2 status were deemed to not be triple negative

		ALL PATIENTS (n = 206)
HER2	N (%) Positive	33 (16.0)
	Unknown	14 (6.8)
Triple-Negative	N (%) Positive	26 (12.6)*
Treatment and Follow-Up		
Surgery	N (%) Mastectomy	114 (55.3)
	Lumpectomy	91 (44.2)
	Axillary Dissection	1 (0.5)
Neoadjuvant Chemotherapy	N (%) Yes	24 (11.7)
Neoadjuvant Hormonal Therapy	N (%) Yes	3 (1.5)
Adjuvant Chemotherapy	N (%) Yes	113 (54.9)
Her2 Treatment	N (%) Yes	25 (12.1)
Bisphosphonates	N (%) Yes	4 (1.9)
Endocrine Therapy	N (%) Yes	159 (77.2)
Radiotherapy	N (%) Yes	159 (77.2)
PCP vs NP Stream	N (%) PCP	124 (60.2)
	NP	79 (38.4)
	GP	1 (0.5)
	N/A	2 (1.0)
Reason for Re-entry into WBCP	N (%) New Primary	30 (14.6)
	Recurrence	176 (85.4)
Type of Recurrence	N (%) Distant	135 (65.5)
	Local	41 (19.9)
	New Primary	30 (14.6)

‡ abdominal pain or abdominal distension

* Patients with unknown Her2 status were deemed to not be triple negative

		ALL PATIENTS (n = 206)
How was Recurrence Detected	N (%) Patient	152 (73.8)
	Imaging	51 (24.8)
	Health Care Provider	2 (1.0)
	Intraoperatively	1 (0.5)
Sites of Metastases	N (%) Axilla	10 (4.9)
	Bone	78 (37.9)
	Lung	17 (8.3)
	Liver	27 (13.1)
	Pelvis	1 (0.5)
	Nodes	4 (1.9)
	Pleura	8 (3.9)
	Peritoneal	1 (0.5)
	Skin	4 (1.9)
	Breast	13 (6.3)
Symptoms	N (%) Bone Pain	51 (24.8)
	Abdominal	22 (10.7)
	Edema	1 (0.5)
	Nausea	3 (1.5)
	Vomiting	2 (1.0)
	Cough	8 (3.9)
	Dyspnea	19 (9.2)
	Fatigue	4 (1.9)
	Anorexia	5 (2.4)
Years to Recurrence	Median (range)	4.6 (0.8, 17.7)
	NA	18
‡ abdominal pain or abdominal distension		
* Patients with unknown Her2 status were deemed to not be triple negative		

Table 2
Patient's characteristics stratified by type of recurrence

		Local	Distant	Contralateral
N		41	135	30
How was Recurrence Detected	N (%) Patient	22 (53.7)	125 (92.6)	5 (16.7)
	Imaging	17 (41.5)	9 (6.7)	25 (83.3)
	Health Care Provider	1 (2.4)	1 (0.7)	0
	Intraoperatively	1 (2.4)	0	0
Sites of Metastases	N (%) Axilla	9 (22.0)	1 (0.7)	0
	Bone	0	78 (57.8)	0
	Lung	0	1 (12.6)	0
	Liver	0	27 (20.0)	0
	Pelvis	0	1 (0.7)	0
	Nodes	0	4 (3.0)	0
	Pleura	0	8 (5.9)	0
	Peritoneal	0	1 (0.7)	0
	Skin	0	4 (3.0)	0
	Breast	7 (17.1)	2 (1.5)	4 (13.3)
Symptoms	N (%) Bone Pain	0	44 (32.6)	1 (3.3)
	Axillary/Breast Pain	6 (14.6)	0	0
	Abdominal	0	22 (16.3)	0
	Edema	0	1 (0.7)	0
	Nausea	0	3 (2.2)	0
	Vomiting	0	2 (1.5)	0
	Cough	0	8 (5.9)	0
	Dyspnea	0	19 (14.1)	0
	Fatigue	0	4 (3.0)	0
	Anorexia	0	5 (3.7)	0
	ER+	165	110 (81.5)	23 (76.7)

		Local	Distant	Contralateral
PR+	146	95 (70.4)	22 (73.3)	29 (70.7)
ER+ or PR+	170	115 (85.2)	23 (76.7)	32 (78.1)
ER-/PR-/Her2+	9	4 (3.0)	3 (10.0)	2 (4.9)
Triple-Negative	26	16 (11.9)	3 (10.0)	7 (17.1)
Age < 60	104	66 (48.9)	17 (56.7)	21 (51.2)
Age ≥ 60	102	69 (51.1)	13 (43.3)	20 (48.8)
Grade = 1	28	15 (11.6)	7 (24.1)	6 (15.4)
Grade = 2	80	47 (36.4)	15 (51.7)	18 (46.2)
Grade = 3	89	67 (51.9)	7 (24.1)	15 (38.5)
Lumpectomy	91	58 (43.0)	15 (50.0)	18 (43.9)
Mastectomy	114	77 (57.0)	14 (46.7)	23 (56.1)
Adjuvant Chemo	113	84 (62.2)	12 (40.0)	17 (41.5)
Radiotherapy	159	110 (81.5)	23 (76.7)	26 (63.4)
Ductal	167	105 (77.8)	27 (90.0)	35 (85.4)
Lobular	29	23 (17.0)	3 (10.0)	3 (7.3)
Mixed	6	5 (3.7)	0	1 (2.4)
Years to Recurrence	Median (range)	3.9 (0.9, 17.4)	4.6 (0.8, 17.7)	6.5 (1.2, 16.4)

Table 3
Patient's characteristics stratified by mode of recurrence detection

Subgroup	N	Health Care Provider	Imaging	Self
N	205	2 (1.0)	51 (24.9)	152 (74.2)
ER+	165	2 (100)	45 (88.2)	118 (77.6)
PR+	146	1 (50)	41 (80.4)	104 (68.4)
ER + or PR+	170	2 (100)	45 (88.2)	123 (80.9)
ER-/PR-/Her2+	9	0	3 (5.9)	6 (4.0)
Triple-Negative	25	0	2 (3.9)	23 (15.1)
Age < 60	103	0	29 (56.9)	74 (48.7)
Age ≥ 60	102	2 (100)	22 (43.1)	78 (51.3)
New Primary	30	0	25 (49.0)	5 (3.3)
Recurrence	175	2 (100)	26 (51.0)	147 (96.7)
Grade = 1	28	1 (50)	7 (14.3)	20 (13.8)
Grade = 2	80	0	29 (59.2)	51 (35.2)
Grade = 3	88	1 (50)	13 (26.5)	74 (51.0)
Lumpectomy	91	1 (50)	26 (51.0)	64 (42.1)
Mastectomy	113	1 (50)	24 (47.1)	88 (57.9)
Adjuvant Chemo	112	0	25 (49.0)	87 (57.2)
Radiotherapy	158	1 (50)	41 (80.4)	116 (76.3)
Ductal	166	2 (100)	43 (84.3)	121 (79.6)
Lobular	29	0	6 (11.8)	23 (15.1)
Mixed	6	0	0	6 (4.0)

Table 4

		Image Detected	Self-Detected	p-value
N		51	152	
Age	Mean (sd)	58.5 (10.2)	59.1 (13.0)	0.61
	Median (range)	58 (39–82)	61 (25–90)	
Detection of primary cancer	N (%) Self-detected	25 (49.0)	111 (73.0)	0.006
	Screen	24 (47.1)	36 (23.7)	
	NA	2 (3.9)	5 (3.3)	
Histology	Ductal	43 (84.3)	121 (79.6)	0.24
	Lobular	6 (11.8)	23 (15.1)	
	Mixed	0	6 (4.0)	
	DCIS	1 (2.0)	0	
	Other	1 (2.0)	2 (1.3)	
Grade	1	7 (14.3)	20 (13.8)	0.007
	2	29 (59.2)	51 (35.2)	
	3	13 (26.5)	74 (51.0)	
N Stage	0	27 (52.9)	60 (39.5)	0.40
	1	13 (25.5)	56 (36.8)	
	2	6 (11.8)	20 (13.2)	
	3	3 (5.9)	13 (8.6)	
	NX	2 (3.9)	3 (2.0)	
Size (cm)	Median (range)	2.2 (0.2–11.0)	2.5 (0–14)	0.34
ER	N (%) Positive	45 (88.2)	118 (77.6)	0.10
PR	N (%) Positive	41 (80.4)	104 (68.4)	0.10
HER2	N (%) Positive	5 (9.8)	28 (18.4)	0.04
	Unknown	7 (13.7)	7 (4.6)	
Triple-Negative	N (%) Positive	2 (3.9)	23 (15.1)	0.03

		Image Detected	Self-Detected	p-value
Surgery	N (%) Mastectomy	24 (47.1)	88 (57.9)	0.11
	Lumpectomy	26 (51.0)	64 (42.1)	
	Axillary Dissection	1 (2.0)	0	
Neoadjuvant Chemotherapy	N (%) Yes	5 (9.8)	18 (11.8)	0.69
Neoadjuvant Hormonal Therapy	N (%) Yes	1 (2.0)	2 (1.3)	0.74
Adjuvant Chemotherapy	N (%) Yes	25 (49.0)	87 (57.2)	0.31
Her2 Treatment	N (%) Yes	3 (5.9)	22 (14.5)	0.11
Bisphosphonates	N (%) Yes	1 (2.0)	3 (2.0)	0.99
Endocrine Therapy	N (%) Yes	40 (78.4)	117 (77.0)	0.83
Radiotherapy	N (%) Yes	41 (80.4)	116 (76.3)	0.55
PCP vs NP Stream	N (%) PCP	33 (64.7)	89 (58.6)	0.70
	NP	18 (35.3)	60 (39.5)	
	GP	0	1 (0.7)	
	N/A	0	2 (1.3)	
Reason for Re-entry into WBCP	N (%) New Primary	25 (49.0)	5 (3.3)	< 0.001
	Recurrence	26 (51.0)	147 (96.7)	
Type of Recurrence	N (%) Distant	9 (17.7)	125 (82.2)	< 0.001
	Local	17 (33.3)	22 (14.5)	
	New Primary	25 (49.0)	5 (3.3)	

		Image Detected	Self-Detected	p-value
Sites of Metastases	N (%) Axilla	0	10 (6.6)	0.061
	Bone	2 (3.9)	76 (50.0)	< 0.001
	Lung	0	17 (11.2)	0.013
	Liver	0	27 (17.8)	0.001
	Pelvis	0	1 (0.7)	0.56
	Nodes	0	4 (2.6)	0.24
	Pleura	0	8 (5.3)	0.095
	Peritoneal	0	1 (0.7)	0.56
	Skin	0	4 (2.6)	0.24
	Breast	0	13 (8.6)	0.031
Symptoms	N (%) Bone Pain	0	51 (33.6)	< 0.001
	Abdominal	0	22 (14.5)	0.004
	Edema	0	1 (0.7)	0.56
	Nausea	0	3 (2.0)	0.31
	Vomiting	0	2 (1.3)	0.41
	Cough	0	8 (5.3)	0.095
	Dyspnea	0	19 (12.5)	0.008
	Fatigue	0	4 (2.6)	0.24
	Anorexia	0	5 (3.3)	0.19
Years to Recurrence	Median (range)	4.1 (0.9, 17.7)	4.6 (0.8, 17.0)	0.75

Sites of Recurrence

Of the 206 recurrences, 41 were ipsilateral breast recurrences (19.9%), 135 were distant recurrences (65.5%), and 30 were new contralateral primaries (14.6%). Of the ipsilateral recurrences, 40 were invasive cancer, and 1 was ductal carcinoma in situ. The average time to recurrence from initial surgery was 3.9 (0.9–17.3) years for local recurrences, 4.6 (0.8–17.7) years for distant recurrences and 6.5 (1.2–16.4) years for new contralateral cancers.

How Recurrence was Detected

While most local breast recurrences were self-detected by patients, 22/41 (53.7%), 17/41 (43.6%) were detected by routine imaging with mammogram, 1/41 (2.4%) was detected during a routine exam, and

1/41 (2.4%) was detected intraoperatively when the patient underwent scar revision for aesthetic purposes. Interestingly, only 2.4% of local recurrences (1/41, 95% CI 0.1–12.9%) and 0.7% of distant recurrences (1/135, 95% CI 0–4.1%) were detected by a healthcare provider during a routinely planned follow-up visit with breast examination. These two recurrences were detected as palpable thickening along a scar and subcutaneous nodules palpable on the chest. The majority of distant recurrences were detected via patient-reported new symptoms (125/135, 92.6%), and the majority of contralateral breast cancers were detected by routine mammographic imaging (25/30, 83.3%), $p < 0.001$. There was a statistical difference in recurrence detection between image detected vs. self-detected in the following factors: grade 3 (26.5% vs 51%, $p < 0.007$), triple negative breast cancer (3.9% vs. 15.1%, $p = 0.03$), and HER2 disease (18.4% vs. 9.8%, $p = 0.04$). By comparing the mode of initial cancer detection with the mode of recurrence detection; we noticed that the majority (111/152, 73%) of patients with self-detected recurrence were self-detected primary tumours, while the patients with image detected recurrence, their initial primary cancer 25/51 (49%) were self-detected vs. 24/51 (47.1%) screen-detected, ($p < 0.01$).

Recurrence Symptoms and Location

The most common sites of distant disease recurrence were bone (78/135, 57.8%), liver (27/135, 20%), lung/pleura (9/135, 18.5%) (Table 2). Sixty percent of patients (46/78) who were found to have bone metastasis presented with bone pain. Fifty-four percent of patients (25/46) who were found to have lung or pleural metastasis presented with cough or dyspnea. Forty-four percent of patients (12/27) who were found to have liver metastasis presented with abdominal pain and distension.

Discussion

With the rapid shift from in-person to virtual assessments of patients with EBC, there have been ongoing concerns from both patients and healthcare providers that the lack of physical examination might lead to delays in detecting recurrences and possibly worse patient outcomes. This study evaluated the detection of recurrence during a six-year period of a survivorship program prior to the COVID-19 pandemic. While the results do not examine other aspects of well follow-up, such as assessment of treatment toxicity, cancer complications, or patient satisfaction, the results are reassuring for patients and healthcare providers as only 2 out of 206 patients had a recurrence detected during a physical examination. In fact, it is estimated that 30,000–35,000 follow-up visits were required for the healthcare providers to detect these 2 recurrences. This seems like an exorbitant use of resources and reinforces that the current guidelines are likely not cost effective. Indeed, these results would suggest that given the frequency of well follow-up that when the pandemic ends, there needs to be a broader evidence-based examination of follow-up care [3].

In the current overview of our own survivorship program, it is apparent that regularly scheduled healthcare provider examination rarely detects recurrence. While the majority of local recurrences were detected through patient-reported symptoms (54.7%), a large number (41.5%) were detected through regular mammographic surveillance. A systematic review in 2007 found that 30–40% of local relapses were

detected through mammograms, which is similar to the results of our analysis[6]. We found that most distant recurrences (92.6%) were detected through symptoms self-reported by patients to their physicians, questioning the utility of the ASCO recommended physical examination every 3–6 months for the first 3 years. Strategies are required to better establish which patients are at higher risk of recurrence, and whether tailored follow-up based on recurrence risk aids in detection. This data is re-assuring that the COVID-19 pandemic and reduction of in-person well follow-up has likely not impacted recurrence detection, and that routine mammographic screening is necessary to continue despite the pandemic.

The strength of this study is that it is a consecutive review of patients, who were all subjected to routine follow-up as per ASCO guidelines i.e., standard of care. However, as it is a single centre retrospective study, this limits generalization. It is also possible that some patients could have recurred and not been referred back to our cancer centre. The relatively short duration of follow-up is a limitation for the recurrence rate in our study. However, the current rate of recurrence in this group is consistent with the nature of early-stage breast cancer.

Conclusion

Breast cancer follow-up is unique in that guidelines vary, the efficacy of follow-up remains uncertain and there exists conflicts between the expectations and desires from patients. We have demonstrated that the majority of recurrences are not detected during healthcare provider appointments and that the majority of local recurrences were detected by regular mammographic surveillance. Given data from a recent systematic review, as well as the evidence that we have obtained from our own evaluation of our survivorship program, reduced follow-up frequency is unlikely to have an major impact on patient recurrence detection and on-demand follow-up or risk-based follow-up presents an appropriate alternative to lower cost-per-recurrence but also to provide patients with reassurance and advance a patient's full return into "wellness"[3]. Prospective analyses looking at the impact of the COVID-19 pandemic on breast cancer recurrence is needed. This will likely corroborate our results that recurrence is not detected by routine follow-up visits and that future prospective trials examining risk-based follow-up are needed.

Declarations

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This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ottawa Hospital Science Network Research Ethics Board (OHSN-REB).

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request and approval from the OHSN-REB.

All authors contributed to the study conception and design. Material preparation, and data collection were performed by Ana-Alicia Beltran-Bless, Bader Alshamsan, Mashari Jemaan Alzahrani, Kelly-Anne Baines,

Vicky Samuel and Gail Larocque. Analysis was conducted by Gregory Pond The first draft of the manuscript was written by Ana-Alicia Beltran-Bless and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figures

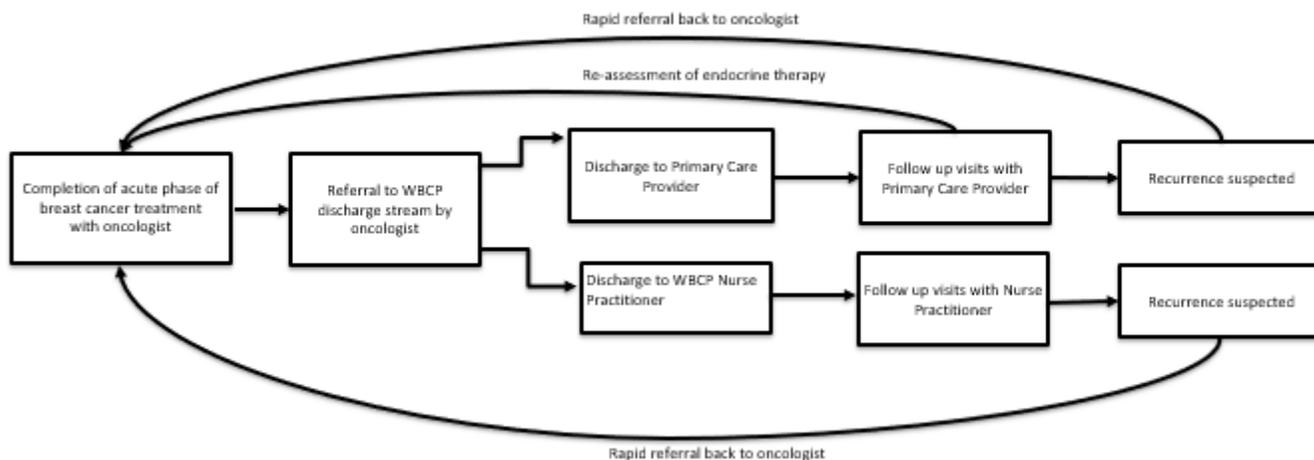


Figure 1

WBCP Follow-up model

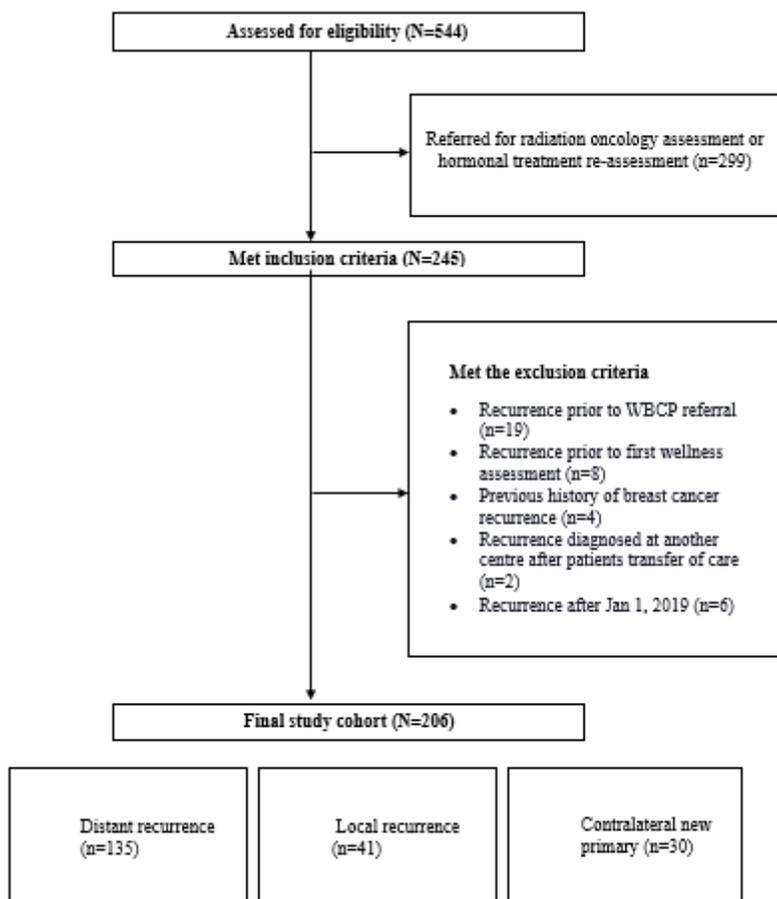


Figure 2

Study schema

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