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Research

Differences in breast cancer diagnosis by patient presentation in Ontario: a retrospective cohort study

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Abstract

Background: In Ontario, patients with breast cancer typically receive their diagnoses through the Ontario Breast Screening Program (OBSP) after an abnormal screen, through screening initiated by a primary care provider or other referring physician, or through follow-up of symptoms by patients' primary care providers. We sought to explore the association of the route to diagnosis (screening within or outside the OBSP or via symptomatic presentation) with use of OBSP-affiliated breast assessment sites (O-BAS), wait times until diagnosis or treatment, health care use and overall survival for patients with breast cancer.

Methods: In this retrospective cohort study, we used the Ontario Cancer Registry to identify adults (aged 18–105 yr) who received a diagnosis of breast cancer from 2013 to 2017. We excluded patients if they were not Ontario residents or had missing age or sex, or who died before diagnosis. We used logistic regression to evaluate factors associated with categorical variables (whether patients were or were not referred to an OBAS, whether patients were screened or symptomatic) and Cox proportional hazards regression to identify factors associated with all-cause mortality.

Results: Of 51 460 patients with breast cancer, 42 598 (83%) received their diagnoses at an O-BAS. Patients whose cancer was first detected through the OBSP were more likely than symptomatic patients to be given a diagnosis at an O-BAS (adjusted odds ratio 1.68, 95% confidence interval [CI] 1.57 to 1.80). Patients screened by the OBSP were given their diagnoses 1 month earlier than symptomatic patients, but diagnosis at an O-BAS did not affect the time until either diagnosis or treatment. Patients referred to an O-BAS had significantly better overall survival than those who were not referred (adjusted hazard ratio 0.73, 95% CI 0.66 to 0.80).

Interpretation: Patients screened through the OBSP were given their diagnoses earlier than symptomatic patients and were more likely to be referred to an O-BAS, which was associated with better survival. Our findings suggest that individuals with signs and symptoms of breast cancer would benefit from similar referral processes, oversight and standards to those used by the OBSP.

Breast cancer is the second most common malignant disease, accounting for 12% of all cancers worldwide.[1,2] Given the large number of patients with breast cancer, inefficiencies in care are expected to affect many patients and health care resources. In an effort to improve the timeliness, efficiency and patient outcomes of assessment for breast cancer, Ontario Health (Cancer Care Ontario) designated certain facilities as breast assessment sites, affiliated with the Ontario Breast Screening Program (OBSP).[3–5] To qualify, facilities are required to have a patient navigation system that coordinates referrals through a defined clinical pathway and have access to diagnostic imaging, image-guided biopsies, and pathology and surgical services.[3–7] Although these OBSP-affiliated breast assessment sites (O-BAS) are affiliated with the OBSP, symptomatic women may also be referred directly to an O-BAS.

Typically, patients with a diagnosis of breast cancer first engage the health care system through their primary care provider with a symptomatic presentation (e.g., finding a lump, nipple discharge, inflammation or pain) or through screening within the OBSP.[8,9] Some patients may be given their diagnosis after screening was initiated by their primary care provider, rather than through the OBSP. Given the relation between the OBSP and O-BAS, we expect fewer symptomatic women to receive their diagnosis from an O-BAS. Moreover, we expect the diagnostic process to be less efficient for symptomatic patients whose primary care provider coordinates the diagnostic work-up.

Competing interests: Steven Habbous, Esha Homenauth, Andriana Barisic, Sharmilaa Kandasamy, Vicky Majpruz, Katharina Forster, Marta Yurcan, Anna Chiarelli, Claire Holloway and Andrea Eisen are employees or consultants of Ontario Health (Cancer Care Ontario), which funds the Ontario Breast Screening Program. No other competing interests were declared.

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In the present study, we explored the association of the route to diagnosis (screening within or outside the OBSP or via symptomatic presentation) with use of O-BAS, wait times until diagnosis or treatment, health care use and overall survival for patients with breast cancer.

Methods

Study design and setting

We conducted a retrospective population-based cohort study of patients in Ontario, Canada, where health care is provisioned under a single-payer system. We reported data in accordance with the Reporting of Studies Conducted Using Observational Routinely Collected Health Data (RECORD) checklist.[10]

The OBSP has operated since 1990 to deliver organized, population-based breast screening to eligible women aged 50–74 years.[11] Men are not eligible for the program. Women are ineligible if they have previously had breast cancer or augmentation mammoplasty, or if they currently have acute breast symptoms. Although most women are screened biennially, those at increased risk of breast cancer are screened annually. The OBSP was expanded in July 2011 to screen women aged 30–69 years at high risk for breast cancer with annual digital mammography and magnetic resonance imaging (MRI), or with ultrasonography if MRI is contraindicated.[12] Women who meet at least 1 of the high-risk criteria are eligible for screening (https://www.cancercareontario.ca/en/guidelines-advice/cancer-continuum/screening/breast-cancer-high-risk-women), even if they have a history of breast or other cancers, breast implants or unilateral mastectomy.

Participants

We included adult (aged 18–105 yr) patients with breast cancer who received their diagnoses in Ontario, Canada, from Jan. 1, 2013, to Dec. 31, 2017. We identified patients from the Ontario Cancer Registry using the site code C50 for breast cancer, with the behaviour code 3 (indicating primary invasive breast cancer) *International Classification of Diseases for Oncology, 3rd edition*. We included patients who had a valid Ontario health insurance number and postal code, and who accessed the Ontario Health Insurance Program (OHIP) within 1 year of the diagnosis date. We omitted patients who died before or on the diagnosis date, whose breast cancer was diagnosed by autopsy or who were missing age or sex.

Data sources

We identified patients with breast cancer and their date or fact of death from the Ontario Cancer Registry and the Registered Persons Database. We used the Integrated Client Management System (ICMS) to identify patients whose breast cancer was first detected through the OBSP, as well to determine whether these patients were referred to an O-BAS.

We captured measures of health care use and wait times using the physician billing (OHIP) database, the hospital admissions database (Discharge Abstract Database [DAD]) and the outpatient hospital database (National Ambulatory Care Reporting System [NACRS]).[13,14] We used the Collaborative Staging database for staging and biomarker status.[15] We used the Ontario Cancer Registry to identify topography (i.e., site of origin) and histology (Appendix 1, eTable S1, available at www.cmajopen.ca/content/10/2/E313/suppl/DC1).

We derived sociodemographic characteristics from the Census using the Postal Code Conversion File+ (version 7B for income and rurality, 2016 Census; version 6C for immigrant density, 2006 Census).[16] We obtained treatment information from the OHIP, DAD, NACRS, Activity Level Reporting New Drug Funding Program (NDFP) and Ontario Drug Benefits databases.[17] We linked databases using health insurance numbers. All databases employed are used for continuous system performance monitoring and undergo routine quality checks.

Exposure

We used the ICMS database to classify patients as OBSP-screened if their OBSP-initiated screening led to their breast cancer diagnosis, or as non-OBSP-screened if they had a screening mammogram in the OHIP database less than 12 months before diagnosis (Figure 1). We classified the remaining patients as symptomatic, who we presume engaged the health care system because they discovered a breast lump, or had breast pain, nipple discharge or inflammation.[8] Non-OBSP-screened and symptomatic patients may have been screened more than 12 months previously through the OBSP, but this earlier screen did not lead to the breast cancer diagnosed during the study period.

We used the ICMS to identify whether OBSP-screened patients were assessed at an O-BAS (Appendix 1, eTable S2). To determine whether non-OBSP-screened and symptomatic patients were assessed at an O-BAS, we used the location of the patient's biopsy from billing data, supplemented with the location of the patient's surgery (OHIP).[9,18]

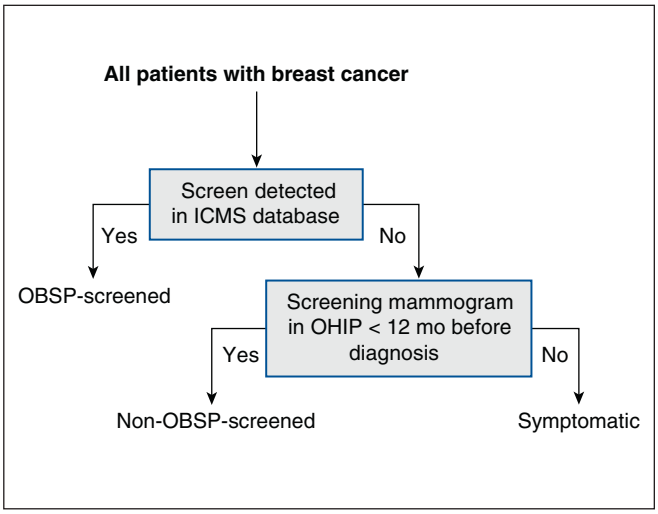

Figure 1: Categorization of patients as screened through the Ontario Breast Screening Program (OBSP-screened), screened outside the OBSP (non-OBSP-screened) or symptomatic. Note: ICMS = Integrated Client Management System, OHIP = Ontario Health Insurance Plan.

Covariates

We used the Collaborative Staging database to identify overall cancer stage[19] and the tumours' estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 status. We used DAD and NACRS to estimate comorbidity using the Charlson Comorbidity Index, with a window of 3 years before the diagnosis date, excluding cancer (Appendix 1, eFigure S1).[20,21] We also included sociodemographic characteristics such as neighbourhood income quintile, rurality and neighbourhood immigrant density, as well as Local Health Integration Network (LHIN), which are crown agencies established by the Government of Ontario to plan, coordinate, integrate and fund health services at a local level (e.g., hospitals). To assign a patient to a specific LHIN, we used the postal code of their residence at the time of diagnosis.

Outcomes

As a measure of efficiency, we estimated the time from suspicion of breast cancer until diagnosis (diagnostic interval). For screen-detected cancers, the time of suspicion was the date of the screening test, identified from ICMS (OBSP-screened patients) or of the screening mammogram from OHIP (non-OBSP-screened patients). For symptomatic patients, we searched OHIP, DAD and NACRS for relevant encounters and diagnostic codes using methodology published elsewhere (Appendix 1, eTable S3).[22,23]

We also estimated the time from diagnosis to start of treatment (pretreatment interval) using the earliest date of breast resection (Appendix 1, eTable S3), antineoplastic systemic therapy (identified from DAD, NACRS, Activity Level Reporting, NDFP and Ontario Drug Benefits) or chest radiation (identified from Activity Level Reporting). We also explored the frequency and timing of diagnostic tests, consultations and visits with health care providers from 6 months before diagnosis until the date of first treatment using OHIP, DAD and NACRS (Appendix 1, eTables S4–5).

As a measure of effectiveness, we measured overall patient survival. The follow-up period started at the time of diagnosis and ended at death (from the Ontario Cancer Registry, supplemented with the Registered Persons Database) or the last known health care encounter until Dec. 31, 2019.

Statistical analysis

We used bivariate or multinomial logistic regression to compare factors between groups, reporting odds ratios (ORs) and 95% confidence intervals (CIs). We used linear regression to explore factors associated with wait times, reporting β coefficients and 95% CIs, which represent the change in days per unit change in the covariate. We confirmed the absence of heteroscedasticity using the autoreg procedure in SAS. We used Cox proportional hazards regression to explore factors associated with all-cause mortality, reporting hazard ratios (HRs) and 95% CIs. For OBSP-screened patients, we corrected lead-time bias by subtracting $(1–\exp[–\lambda t])/\lambda$ from each patient's survival time, where λ is the inverse of the mean sojourn time (24 mo, the average time for an asymptomatic patient to become symptomatic) and t is the survival time.[24]

Unless otherwise stated, we adjusted all multivariable models for O-BAS status, screened or symptomatic presentation, age, sex, neighbourhood income quintile, neighbourhood immigrant density, rurality, Charlson Comorbidity Index, previous breast or other cancer, laterality, stage, hormone receptor profile, topography, histology and geography (Local Health Integration Network). These covariates were chosen because of data availability, their perceived clinical importance and their potential to control for known or unknown confounders.[25,26]

We confirmed proportionality by visual inspection of Kaplan–Meier plots, log(–log) survival plots and Loess-smoothed Schoenfeld residuals versus time. We performed all analyses using SAS version 9.4 (SAS Institute Inc.). Statistical tests were 2-sided and evaluated at a 5% significance level. We suppressed all cells less than 6.

Ethics approval

Ethics approval was not required because this work was done for the purposes of health system improvement and aligns with Cancer Care Ontario's role as a prescribed entity under Section 45 of Ontario's *Personal Health Information Protection Act*.

Results

We identified a total of 51 460 patients with breast cancer (Appendix 1, eFigure S2). The mean age at diagnosis was 63 (standard deviation [SD] 13.7) years, 44 382 (86.2%) had no comorbidity, 3845 (7.5%) had a previous breast cancer and 42 598 (82.8%) were given their breast cancer diagnosis at an O-BAS (Table 1). A total of 28 107 (54.6%) patients were symptomatic, 13 615 (26.5%) were OBSP-screened and 9738 (18.9%) were non-OBSP-screened.

Referral to an O-BAS

After adjustment, patients referred to an O-BAS were more likely to be younger, have no comorbidities, live closer to an O-BAS and live in a higher-income urban neighbourhood ($p < 0.001$ for all) (Table 1). Patients referred to an O-BAS had lower-stage disease ($p < 0.0001$), known hormone receptor status ($p < 0.0001$), a greater risk of previous breast cancer ($p = 0.0005$) and were more likely to have had an OBSP-screened cancer (OR 1.68, 95% CI 1.57 to 1.80) or non-OBSP-screened cancer (OR 1.32, 95% CI 1.23 to 1.41) than to be symptomatic.

Route of cancer detection

The proportion of patients who were OBSP-screened increased from 22.9% in 2013 to 28.8% in 2017, with correspondingly fewer patients presenting with symptoms (Figure 2). Symptomatic patients were more likely to reside in a lower-income neighbourhood ($p < 0.0001$) and have more comorbidities ($p < 0.0001$). They were also more likely to have

Table 1 (part 1 of 3): Sociodemographic, clinical and tumour characteristics of patients with breast cancer who were or were not referred to a Breast Assessment Site affiliated with the Ontario Breast Screening Program

Characteristic	No. (%) of patients*		O-BAS v. non-O-BAS Bivariate		O-BAS v. non-O-BAS Multivariable†	
	Non-O-BAS *n* = 8862	O-BAS *n* = 42 598	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Screening status				< 0.0001		< 0.0001
Symptomatic	5908 (66.7)	22 199 (52.1)	Ref.		Ref.	
Non-OBSP-screened	1477 (16.7)	8261 (19.4)	1.49 (1.40 to 1.58)		1.32 (1.23 to 1.41)	
OBSP-screened	1477 (16.7)	12 138 (28.5)	2.19 (2.06 to 2.33)		1.68 (1.57 to 1.80)	
Sociodemographic						
Sex						
Female	8750 (98.7)	42 285 (99.3)	Ref.		Ref.	
Male	112 (1.3)	313 (0.7)	0.58 (0.47 to 0.72)		0.93 (0.73 to 1.19)	
Age, yr, mean ± SD (OR per 10-yr increment)	66 ± 14.6	63 ± 13.5	0.87 (0.85 to 0.88)		0.88 (0.86 to 0.90)	
Age, yr				< 0.0001		< 0.0001
< 50	1328 (15.0)	7244 (17.0)	Ref.			
50–74	4833 (54.5)	26 048 (61.1)	0.99 (0.93 to 1.06)			
> 74	2701 (30.5)	9306 (21.8)	0.63 (0.59 to 0.68)			
After-tax neighbourhood income quintile‡				< 0.0001		< 0.0001
Highest	1756 (19.9)	9368 (22.2)	Ref.		Ref.	
Mid-high	1640 (18.6)	8235 (19.5)	0.94 (0.88 to 1.01)		0.91 (0.84 to 0.99)	
Middle	1678 (19.1)	8291 (19.7)	0.93 (0.86 to 1.00)		0.93 (0.85 to 1.00)	
Mid-low	1797 (20.4)	8539 (20.3)	0.89 (0.83 to 0.96)		0.88 (0.81 to 0.95)	
Lowest	1933 (22.0)	7695 (18.3)	0.75 (0.70 to 0.80)		0.77 (0.70 to 0.83)	
Neighbourhood immigrant density‡				0.004		0.0002
Least dense	5221 (59.4)	24 537 (58.1)	Ref.		Ref.	
Mid-dense	2068 (23.5)	10 661 (25.2)	1.10 (1.04 to 1.16)		1.09 (1.01 to 1.17)	
Most dense	1497 (17.0)	7061 (16.7)	1.00 (0.94 to 1.07)		0.91 (0.83 to 1.00)	
Rurality‡						
Urban	7479 (84.9)	37 789 (89.7)	Ref.		Ref.	
Rural	1326 (15.1)	4351 (10.3)	0.65 (0.61 to 0.69)		0.65 (0.59 to 0.71)	
Distance to closest O-BAS, km, mean ± SD (OR per 100-km increment)§	15.7 ± 21.6	11.9 ± 19.2	0.44 (0.40 to 0.49)		0.36 (0.31 to 0.42)	
Clinical						
Charlson Comorbidity Index				< 0.0001		0.0002
Missing	3011 (34.0)	16 228 (38.1)	1.12 (1.06 to 1.18)		1.04 (0.98 to 1.10)	
0	4318 (48.7)	20 825 (48.9)	Ref.		Ref.	
1	935 (10.6)	3665 (8.6)	0.81 (0.75 to 0.88)		0.89 (0.82 to 0.97)	
2	316 (3.6)	1088 (2.6)	0.71 (0.63 to 0.81)		0.88 (0.76 to 1.01)	
≥ 3	282 (3.2)	792 (1.9)	0.58 (0.51 to 0.67)		0.78 (0.66 to 0.91)	
Previous breast cancer relative to diagnosis, yr				< 0.0001		0.0005
Never	8074 (91.1)	39 541 (92.8)	Ref.		Ref.	
≤ 5	72 (0.8)	250 (0.6)	0.71 (0.55 to 0.92)		1.06 (0.79 to 1.41)	
5–10	239 (2.7)	852 (2.0)	0.73 (0.63 to 0.84)		1.21 (1.03 to 1.43)	
≥ 10	477 (5.4)	1955 (4.6)	0.84 (0.76 to 0.93)		1.25 (1.11 to 1.41)	

Table 1 (part 2 of 3): Sociodemographic, clinical and tumour characteristics of patients with breast cancer who were or were not referred to a Breast Assessment Site affiliated with the Ontario Breast Screening Program

Characteristic	No. (%) of patients*		O-BAS v. non-O-BAS Bivariate		O-BAS v. non-O-BAS Multivariable†	
	Non-O-BAS *n* = 8862	O-BAS *n* = 42 598	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Previous other cancer relative to diagnosis, yr				< 0.0001		0.15
Never	8180 (92.3)	39 563 (92.9)	Ref.		Ref.	
≤ 5	295 (3.3)	1172 (2.8)	0.82 (0.72 to 0.94)		1.01 (0.87 to 1.17)	
5–10	136 (1.5)	686 (1.6)	1.04 (0.87 to 1.26)		1.22 (1.00 to 1.50)	
≥ 10	251 (2.8)	1177 (2.8)	0.97 (0.84 to 1.11)		1.11 (0.95 to 1.29)	
Cancer						
Laterality				0.47		0.03
Right	4288 (48.4)	20 701 (48.7)	Ref.		Ref.	
Left	4329 (49.9)	21 516 (50.6)	1.03 (0.98 to 1.08)		1.02 (0.97 to 1.08)	
Bilateral	65 (0.7)	319 (0.7)	1.02 (0.78 to 1.33)		1.47 (1.09 to 1.98)	
Cancer stage				< 0.0001		< 0.0001
0	28 (0.3)	171 (0.4)	0.91 (0.61 to 1.36)		1.57 (1.02 to 2.42)	
1	2755 (31.7)	18 463 (44.1)	Ref.		Ref.	
2	2861 (32.9)	15 707 (37.5)	0.82 (0.77 to 0.87)		0.91 (0.85 to 0.97)	
3	1134 (13.0)	5023 (12.0)	0.66 (0.61 to 0.71)		0.75 (0.69 to 0.82)	
4	1085 (12.5)	1343 (3.2)	0.19 (0.17 to 0.20)		0.23 (0.21 to 0.26)	
Unknown	832 (9.6)	1167 (2.8)	0.21 (0.19 to 0.23)		0.37 (0.32 to 0.42)	
Histology				< 0.0001		< 0.0001
Ductal	6254 (70.6)	32 661 (76.7)	Ref.		Ref.	
Lobular	800 (9.0)	3689 (8.7)	0.88 (0.81 to 0.96)		1.00 (0.92 to 1.10)	
Ductal and lobular	298 (3.4)	1894 (4.4)	1.21 (1.07 to 1.38)		1.20 (1.05 to 1.38)	
Adenocarcinoma	366 (4.1)	930 (2.2)	0.49 (0.43 to 0.55)		0.73 (0.62 to 0.84)	
Mucinous	157 (1.8)	797 (1.9)	0.97 (0.82 to 1.16)		1.02 (0.84 to 1.23)	
Other	987 (11.1)	2627 (6.2)	0.51 (0.47 to 0.55)		0.89 (0.81 to 0.98)	
Hormone receptor profile				0.08		< 0.0001
ER–, PR–, HER2–	679 (7.7)	3814 (9.0)	Ref.		Ref.	
ER–, PR–, HER2+	325 (3.7)	1807 (4.2)	0.99 (0.86 to 1.14)		1.02 (0.88 to 1.20)	
ER–, PR+, HER2–	36 (0.4)	182 (0.4)	0.90 (0.62 to 1.30)		1.10 (0.75 to 1.64)	
ER–, PR+, HER2+	20 (0.2)	69 (0.2)	0.61 (0.37 to 1.02)		0.91 (0.53 to 1.57)	
ER+, PR–, HER2–	561 (6.3)	2751 (6.5)	0.87 (0.77 to 0.99)		0.87 (0.76 to 0.99)	
ER+, PR–, HER2+	204 (2.3)	1036 (2.4)	0.90 (0.76 to 1.07)		0.94 (0.78 to 1.13)	
ER+, PR+, HER2–	4379 (49.4)	24 116 (56.6)	0.98 (0.90 to 1.07)		0.90 (0.82 to 0.99)	
ER+, PR+, HER2+	473 (5.3)	2773 (6.5)	1.04 (0.92 to 1.19)		0.97 (0.85 to 1.11)	
Missing	2185 (24.7)	6050 (14.2)	0.49 (0.45 to 0.54)		0.66 (0.59 to 0.74)	
Topography				< 0.0001		< 0.0001
Upper–outer quadrant	2754 (31.1)	15 672 (36.8)	Ref.		Ref.	
Breast NOS	1452 (16.4)	3411 (8.0)	0.41 (0.38 to 0.44)		0.70 (0.64 to 0.76)	
Overlapping lesion	1618 (18.3)	7720 (18.1)	0.84 (0.78 to 0.90)		0.93 (0.87 to 1.00)	
Upper–inner quadrant	1007 (11.4)	5806 (13.6)	1.01 (0.94 to 1.10)		0.98 (0.90 to 1.07)	
Lower–outer quadrant	721 (8.1)	4056 (9.5)	0.99 (0.90 to 1.08)		1.00 (0.91 to 1.10)	
Central portion	503 (5.7)	2205 (5.2)	0.77 (0.69 to 0.86)		0.91 (0.81 to 1.02)	
Lower–inner quadrant	470 (5.3)	2558 (6.0)	0.96 (0.86 to 1.06)		0.98 (0.87 to 1.10)	
Nipple	236 (2.7)	922 (2.2)	0.69 (0.59 to 0.80)		0.77 (0.66 to 0.91)	
Axillary tail	101 (1.1)	248 (0.6)	0.43 (0.34 to 0.55)		0.56 (0.43 to 0.72)	

Table 1 (part 3 of 3): Sociodemographic, clinical and tumour characteristics of patients with breast cancer who were or were not referred to a Breast Assessment Site affiliated with the Ontario Breast Screening Program

	No. (%) of patients*		O-BAS v. non-O-BAS Bivariate		O-BAS v. non-O-BAS Multivariable†	
Characteristic	Non-O-BAS *n* = 8862	O-BAS *n* = 42 598	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Other						
Year of diagnosis (row percentages provided)				0.01		0.04
2013	1767 (19.9)	8037 (18.9)	Ref.		Ref.	
2014	1748 (19.7)	8447 (19.8)	1.06 (0.99 to 1.14)		1.03 (0.95 to 1.11)	
2015	1715 (19.4)	8518 (20.0)	1.09 (1.02 to 1.18)		1.03 (0.96 to 1.12)	
2016	1882 (21.2)	8695 (20.4)	1.02 (0.95 to 1.09)		0.98 (0.90 to 1.06)	
2017	1750 (19.7)	8901 (20.9)	1.12 (1.04 to 1.20)		1.10 (1.02 to 1.19)	

Note: CI = confidence interval, ER = estrogen receptor, HER2 = human epidermal growth factor receptor 2, NOS = not otherwise specified, O-BAS = OBSP-affiliated breast assessment site, OBSP = Ontario Breast Screening Program, OR = odds ratio, PR = progesterone receptor, Ref. = reference category, SD = standard deviation.
*Unless indicated otherwise.
†*n* = 49 420; adjusted for screening status, age, neighbourhood income quintile, neighbourhood immigrant density, rurality, distance to the closest O-BAS, Charlson Comorbidity Index, previous breast cancer, previous other cancer, laterality, cancer stage, hormone receptor profile, topography, year of diagnosis and Local Health Integration Network.
‡Adapted from Statistics Canada *Postal Code Conversion File* and *Postal Code Conversion File Plus* (June 2017), which is based on data licensed from Canada Post Corporation.[16] We used the patient's postal code at diagnosis.
§Odds ratio reflects the odds of diagnosis in an O-BAS for every 100-km increase in Euclidean distance to the patient's closest O-BAS. We used the patient's postal code at diagnosis.

advanced-stage breast cancer at diagnosis than screened patients; 8166 (29.1%) of symptomatic patients had stage 1 breast cancer at diagnosis, compared with 4519 (46.5%) of non-OBSP-screened patients and 8523 (62.6%) of OBSP-screened patients (Table 2). Symptomatic patients were more likely to have biologically more aggressive disease; 4319 (15.4%) had tumours negative for estrogen receptor (v. 1337 [9.8%] for OBSP-screened patients) and 4072 (14.5%) had tumours positive for human epidermal growth factor receptor 2 (v. 1429 [10.5%] for OBSP-screened patients).

Diagnostic interval

The diagnostic interval (i.e., time from suspicion of breast cancer until diagnosis) was a median 35 (interquartile range [IQR] 19 to 82) days. Diagnosis at an O-BAS did not meaningfully reduce the diagnostic interval (β –2.0 d, 95% CI –3.6 to –0.3 d) (Table 3) or shorter subintervals (Appendix 1, eTable S6).

Compared with patients with stage 1 cancer, the diagnostic interval was 10, 13, 21 and 9 days shorter for patients with stage 2, 3, 4 and unknown stage, respectively ($p < 0.0001$). Patients with bilateral breast cancer had a shorter diagnostic interval (β –9.7 d, 95% CI –16.3 to –3.0 d) than those with unilateral disease, as did male patients (β –12.6 d, 95% CI –19.3 to –5.9 d) compared with female patients. Compared with symptomatic patients, the diagnostic interval was 25 days shorter (β –24.8 d, 95% CI –26.2 to –23.3 d) for OBSP-screened patients and 5 days longer (β 4.7 d, 95% CI 3.3 to 6.3 d) for non-OBSP-screened patients. No other demographic and clinical factors were meaningfully associated with the length of the diagnostic interval.

Pretreatment interval

The first intervention provided was surgery for 40 652 (79.0%) patients and systemic therapy for 9296 (18.1%) patients. The pretreatment interval (i.e., time from diagnosis to start of treatment) was a median 34 (IQR 23 to 47) days. After adjustment, no factors were associated with a meaningful delay (Table 3).

Health care use

Patients referred to an O-BAS were more likely to have received various diagnostic tests before treatment than those who were not referred, including diagnostic mammography (90.9% v. 78.2%), screening mammography (43.7% v. 30.3%), breast biopsy (96.6% v. 85.1%), breast ultrasonography (94.3% v. 82.1%) and breast MRI (22.6% v. 13.2%) (Table 4). However, patients referred to an O-BAS were less likely to have had abdominal or thoracic computed tomography (24.5% v. 38.0%) and chest radiography (39.3% v. 48.5%). Patients referred to an O-BAS were more likely than those who were not referred to have a consultation with a general surgeon or general thoracic surgeon (97.0% v. 86.8%), but were less likely to visit their primary care provider (40.0% v. 48.9%), have a consultation with an internist (17.7% v. 24.0%) or medical oncologist (14.5% v. 26.0%).

Patients referred to an O-BAS had a consultation or visit with a general surgeon or general thoracic surgeon later than those who were not referred (median 8 d v. 1 d after diagnosis) (Table 4). However, the time from diagnosis until consultation with a medical oncologist or radiation oncologist was longer, with a median 20 (IQR 11 to 32) days and 21 (IQR 10 to 34) days overall, respectively.

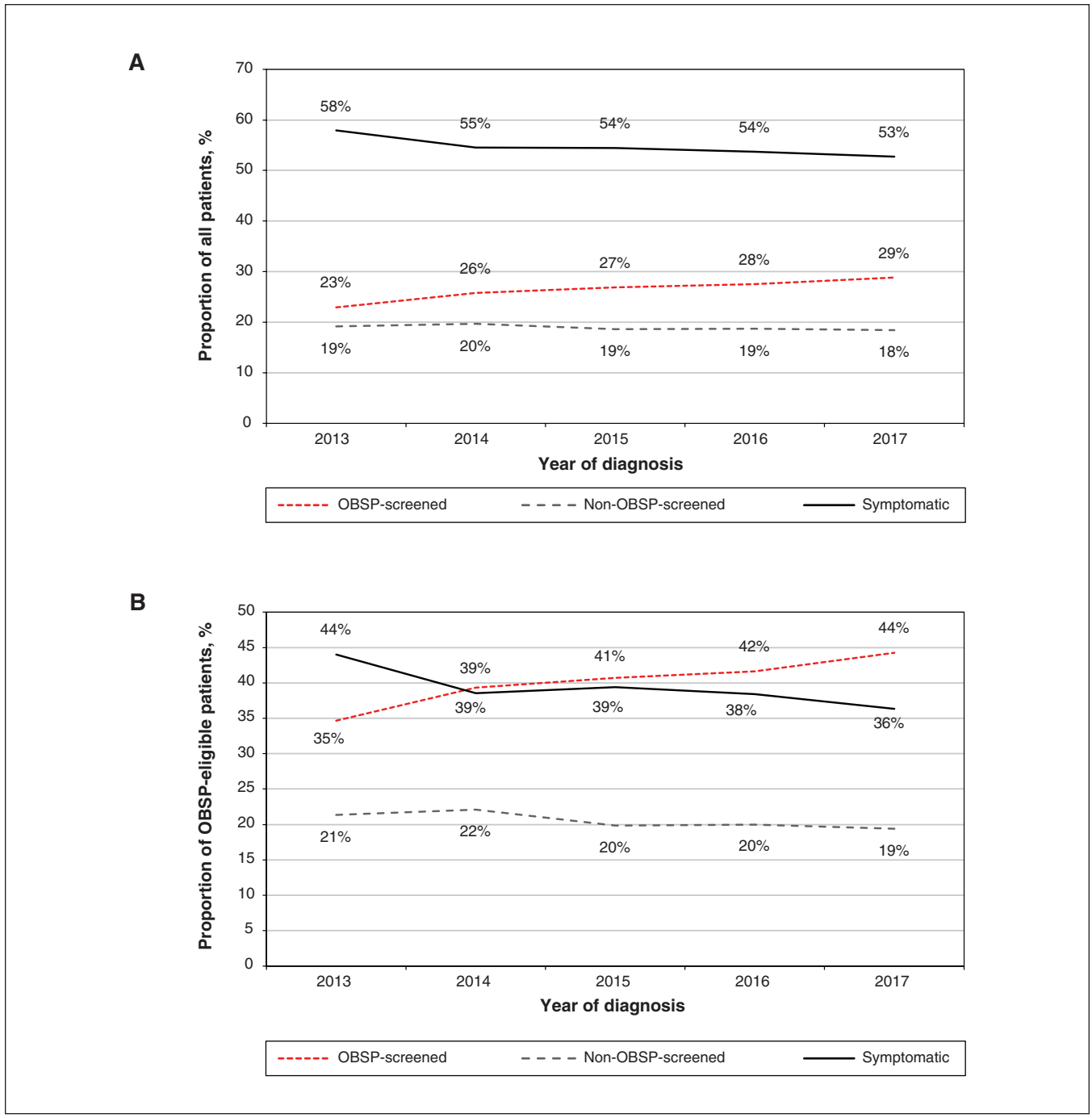

Figure 2: (A) The proportion of all patients with breast cancer whose cancer was detected by screening at an Ontario Breast Screening Program (OBSP-screened), by screening outside an OBSP (non-OBSP-screened) or by symptoms. (B) The proportion of patients with breast cancer presumed to be eligible for OBSP (female patients aged 50–74 yr, no previous breast cancer) whose cancer was detected by screening at an OBSP, by screening outside an OBSP or by symptoms.

Overall survival

Patients were followed for an average of 42 (SD 21.5) months after diagnosis. After adjustment, patients referred to an O-BAS for diagnosis had better overall survival than those who were not (HR 0.72, 95% CI 0.68 to 0.76) (Table 5). Overall survival was also better for patients who were either OBSP-screened (HR 0.72, 95% CI 0.66 to 0.79) or non-OBSP-screened (HR 0.67, 95% CI 0.62 to 0.72), compared with symptomatic patients.

Without adjustment, O-BAS had a larger impact on survival among symptomatic patients (HR 0.43, 95% CI 0.41 to 0.45), and non-OBSP-screened patients (HR 0.48, 95% CI 0.41 to 0.56) than OBSP-screened patients (HR 0.69, 95% CI 0.55 to 0.88) ($p_{interaction}$ = 0.0003) (Figure 3). In the adjusted

Table 2 (part 1 of 3): Sociodemographic, clinical and cancer characteristics of patients whose breast cancer was detected by screening or by symptoms

Characteristic	No. (%) of patients			OR (95% CI)*		p value*
	OBSP-screened *n* = 13 615	Non-OBSP-screened *n* = 9738	Symptomatic *n* = 28 107	OBSP-screened v. symptomatic	Non-OBSP-screened v. symptomatic	
O-BAS						< 0.0001
Yes	12 138 (89.2)	8261 (84.8)	22 199 (79.0)	1.74 (1.62 to 1.86)	1.32 (1.23 to 1.41)	
No	1477 (10.8)	1477 (15.2)	5908 (21.0)	Ref.	Ref.	
Sociodemographic						
Sex						< 0.0001
Female	13 615 (100.0)	9714 (99.8)	27 706 (98.6)	NA	0.18 (0.12 to 0.28)	
Male	0 (0.0)	24 (0.3)	401 (1.4)	NA	Ref.	
Age, yr, mean ± SD (OR per 10-yr increment)	63.7 ± 8.0	62.1 ± 12.2	63.4 ± 16.1	1.09 (0.07 to 1.11)	0.96 (0.94 to 0.98)	< 0.0001
Neighbourhood income quintile†						< 0.0001
Highest	3042 (22.6)	2243 (23.3)	5839 (21.0)	Ref.	Ref.	
Mid-high	2727 (20.3)	1943 (20.2)	5205 (18.7)	1.03 (0.96 to 1.11)	0.99 (0.92 to 1.06)	
Middle	2707 (20.1)	1870 (19.4)	5392 (19.4)	1.02 (0.95 to 1.10)	0.95 (0.88 to 1.03)	
Mid to low	2703 (20.1)	1913 (19.9)	5720 (20.5)	0.97 (0.90 to 1.04)	0.94 (0.87 to 1.02)	
Lowest	2275 (16.9)	1667 (17.3)	5686 (20.4)	0.84 (0.78 to 0.91)	0.85 (0.78 to 0.92)	
Neighbourhood immigrant density†						0.07
Least dense	8368 (61.9)	5068 (52.4)	16 322 (58.6)	Ref.	Ref.	
Mid-dense	3124 (23.1)	2704 (28.0)	6901 (24.8)	0.95 (0.89 to 1.01)	1.04 (0.98 to 1.11)	
Most dense	2018 (14.9)	1897 (19.6)	4643 (16.7)	1.01 (0.93 to 1.10)	1.09 (1.00 to 1.19)	
Rurality†						0.01
Urban	11 765 (87.4)	8790 (91.2)	24 713 (88.7)	Ref.	Ref.	
Rural	1693 (12.6)	848 (8.8)	3136 (11.3)	1.14 (1.05 to 1.24)	1,04 (0.94 to 1.15)	
Distance to closest O-BAS, km, mean ± SD (OR per 100-km increment)‡	13.2 ± 20.2	10.8 ± 14.9	12.8 ± 20.8	0.96 (0.83 to 1.11)	0.87 (0.72 to 1.05)	0.32
Clinical						
Charlson Comorbidity Index						< 0.0001
Missing	5328 (39.1)	3839 (39.4)	10 072 (35.8)	1.08 (1.03 to 1.13)	1.04 (0.99 to 1.10)	
0	6738 (49.5)	4784 (49.1)	13 621 (48.5)	Ref.	Ref.	
1	1095 (8.0)	778 (8.0)	2727 (9.7)	0.83 (0.76 to 0.91)	0.91 (0.83 to 0.99)	
2	277 (2.0)	185 (1.9)	942 (3.4)	0.65 (0.56 to 0.76)	0.65 (0.55 to 0.76)	
≥ 3	177 (1.3)	152 (1.6)	745 (2.7)	0.52 (0.43 to 0.63)	0.71 (0.59 to 0.86)	
Previous breast cancer relative to diagnosis, yr						< 0.0001
Never	13 576 (99.7)	8693 (89.3)	25 346 (90.2)	Ref.	Ref.	
≤ 5	< 6	83 (0.9)	235 (0.8)	0.03 (0.01 to 0.08)	0.90 (0.69 to 1.18)	
5–10	17 (0.1)	293 (3.0)	785 (2.8)	0.03 (0.02 to 0.05)	1.01 (0.87 to 1.17)	
≥ 10	22 (0.2)	669 (6.9)	1741 (6.2)	0.02 (0.01 to 0.03)	1.05 (0.95 to 1.16)	
Previous other cancer relative to diagnosis, yr						< 0.0001
Never	12 718 (93.4)	9096 (93.4)	25 929 (92.3)	Ref.	Ref.	
≤ 5	313 (2.3)	269 (2.8)	885 (3.1)	0.63 (0.54 to 0.72)	0.96 (0.83 to 1.11)	
5–10	221 (1.6)	149 (1.5)	452 (1.6)	0.87 (0.73 to 1.04)	1.03 (0.85 to 1.25)	
≥ 10	363 (2.7)	224 (2.3)	841 (3.0)	0.71 (0.63 to 0.82)	0.81 (0.69 to 0.95)	

Table 2 (part 2 of 3): Sociodemographic, clinical and cancer characteristics of patients whose breast cancer was detected by screening or by symptoms

Characteristic	No. (%) of patients			OR (95% CI)*		p value*
	OBSP-screened n = 13 615	Non-OBSP-screened n = 9738	Symptomatic n = 28 107	OBSP-screened v. symptomatic	Non-OBSP-screened v. symptomatic	
Cancer						
Laterality						0.007
Right	6660 (48.9)	4735 (48.8)	13 594 (48.7)	Ref.	Ref.	
Left	6881 (50.6)	4909 (50.6)	14 055 (50.4)	0.99 (0.95 to 1.04)	1.00 (0.95 to 1.05)	
Bilateral	71 (0.5)	61 (0.6)	252 (0.9)	0.59 (0.43 to 0.79)	0.75 (0.56 to 1.01)	
Cancer stage						< 0.0001
0	32 (0.2)	62 (0.6)	105 (0.4)	0.52 (0.34 to 0.79)	0.89 (0.64 to 1.25)	
1	8523 (63.5)	4529 (47.4)	8166 (29.6)	Ref.	Ref.	
2	3859 (28.7)	3235 (33.8)	11 474 (41.6)	0.31 (0.29 to 0.32)	0.50 (0.47 to 0.53)	
3	731 (5.4)	1057 (11.1)	4369 (15.8)	0.16 (0.14 to 0.17)	0.42 (0.39 to 0.46)	
4	97 (0.7)	269 (2.8)	2062 (7.5)	0.06 (0.05 to 0.07)	0.25 (0.22 to 0.29)	
Unknown	185 (1.4)	405 (4.2)	1409 (5.1)	0.27 (0.22 to 0.32)	0.55 (0.48 to 0.64)	
Histology						< 0.0001
Ductal	10 837 (79.6)	7124 (73.2)	20 954 (74.6)	Ref.	Ref.	
Lobular	1213 (8.9)	926 (9.5)	2350 (8.4)	1.16 (1.07 to 1.26)	1.28 (1.18 to 1.40)	
Ductal and lobular	604 (4.4)	441 (4.5)	1147 (4.1)	1.06 (0.95 to 1.19)	1.16 (1.03 to 1.30)	
Adenocarcinoma	292 (2.1)	264 (2.7)	740 (2.6)	1.01 (0.86 to 1.18)	1.22 (1.04 to 1.43)	
Mucinous	224 (1.6)	188 (1.9)	542 (1.9)	0.56 (0.47 to 0.66)	0.90 (0.76 to 1.08)	
Other	445 (3.3)	795 (8.2)	2374 (8.4)	0.59 (0.53 to 0.67)	1.18 (1.07 to 1.30)	
Hormone receptor profile						< 0.0001
ER–, PR–, HER2–	895 (6.6)	822 (8.4)	2776 (9.9)	Ref.	Ref.	
ER–, PR–, HER2+	402 (3.0)	394 (4.0)	1336 (4.8)	0.98 (0.85 to 1.13)	1.02 (0.88 to 1.17)	
ER–, PR+, HER2–	29 (0.2)	45 (0.5)	144 (0.5)	0.63 (0.41 to 0.98)	1.08 (0.76 to 1.54)	
ER–, PR+, HER2+	11 (0.1)	15 (0.2)	63 (0.2)	0.78 (0.40 to 1.53)	0.98 (0.55 to 1.75)	
ER+, PR–, HER2–	923 (6.8)	625 (6.4)	1764 (6.3)	1.47 (1.30 to 1.66)	1.14 (1.01 to 1.29)	
ER+, PR–, HER2+	274 (2.0)	222 (2.3)	744 (2.6)	1.16 (0.98 to 1.37)	1.03 (0.86 to 1.22)	
ER+, PR+, HER2–	8736 (64.2)	5347 (54.9)	14 412 (51.3)	1.45 (1.33 to 1.59)	1.11 (1.02 to 1.21)	
ER+, PR+, HER+	742 (5.4)	575 (5.9)	1929 (6.9)	1.15 (1.02 to 1.30)	1.00 (0.88 to 1.14)	
Missing	1603 (11.8)	1693 (17.4)	4939 (17.6)	1.18 (1.05 to 1.31)	1.16 (1.04 to 1.29)	
Topography						< 0.0001
Upper–outer quadrant	5462 (40.1)	3497 (35.9)	9467 (33.7)	Ref.	Ref.	
Overlapping lesion	2578 (18.9)	1742 (17.9)	5018 (17.9)	0.92 (0.86 to 0.98)	0.97 (0.91 to 1.04)	
Breast NOS	811 (6.0)	876 (9.0)	3176 (11.3)	0.63 (0.57 to 0.69)	0.85 (0.77 to 0.93)	
Lower–outer quadrant	1227 (9.0)	948 (9.7)	2602 (9.3)	0.82 (0.75 to 0.89)	0.99 (0.90 to 1.08)	
Upper–inner quadrant	1986 (14.6)	1260 (12.9)	3567 (12.7)	0.85 (0.79 to 0.91)	0.91 (0.84 to 0.98)	
Lower–inner quadrant	820 (6.0)	578 (5.9)	1630 (5.8)	0.84 (0.76 to 0.93)	0.93 (0.84 to 1.04)	
Central portion	477 (3.5)	539 (5.5)	1692 (6.0)	0.63 (0.56 to 0.71)	1.00 (0.90 to 1.12)	
Nipple	202 (1.5)	233 (2.4)	723 (2.6)	0.58 (0.49 to 0.69)	0.88 (0.75 to 1.04)	
Axillary tail	52 (0.4)	65 (0.7)	232 (0.8)	0.55 (0.39 to 0.76)	0.87 (0.65 to 1.16)	

Table 2 (part 3 of 3): Sociodemographic, clinical and cancer characteristics of patients whose breast cancer was detected by screening or by symptoms

Characteristic	No. (%) of patients			OR (95% CI)*		p value*
	OBSP-screened *n* = 13 615	Non-OBSP-screened *n* = 9738	Symptomatic *n* = 28 107	OBSP-screened v. symptomatic	Non-OBSP-screened v. symptomatic	
Other						
Year of diagnosis (row percentages provided)						< 0.0001
2013	2248 (16.5)	1877 (19.3)	5679 (20.2)	Ref.	Ref.	
2014	2625 (19.3)	2007 (20.6)	5563 (19.8)	1.18 (1.10 to 1.27)	1.09 (1.01 to 1.18)	
2015	2756 (20.2)	1908 (19.6)	5569 (19.8)	1.25 (1.16 to 1.35)	1.03 (0.96 to 1.12)	
2016	2915 (21.4)	1983 (20.4)	5679 (20.2)	1.31 (1.22 to 1.41)	1.06 (0.98 to 1.15)	
2017	3071 (22.6)	1963 (20.2)	5617 (20.0)	1.42 (1.32 to 1.53)	1.06 (0.98 to 1.15)	

Note: CI = confidence interval, ER = estrogen receptor, HER2 = human epidermal growth factor receptor 2, NA = not applicable, NOS = not otherwise specified, O-BAS = OBSP-affiliated breast assessment site, OBSP = Ontario Breast Screening Program, OR = odds ratio, PR = progesterone receptor, Ref. = reference category.
**n* = 49 420; findings derived from a multinomial logistic regression adjusted for all variables in the table and Local Health Information Network. The *p* value is from a single multinomial multivariable model, representing the overall difference between the 3 groups (symptomatic v. OBSP-screened v. non-OBSP-screened), with the symptomatic group as the reference.
†Adapted from Statistics Canada *Postal Code Conversion File* and *Postal Code Conversion File Plus* (June 2017), which is based on data licensed from Canada Post Corporation.[16] We used the patient's postal code at diagnosis.
‡Odds ratios reflect the odds of diagnosis in an O-BAS for every 100-km increase in Euclidean distance to the patient's closest O-BAS. We used the patient's postal code at diagnosis.

model, the difference of the effect of O-BAS on overall survival was similar across patient types ($p_{\text{interaction}}$ = 0.85): HR 0.73 (95% CI 0.69 to 0.78) among symptomatic patients; HR 0.74 (95% CI 0.62 to 0.87) among non-OBSP-screened patients; and HR 0.73 (95% CI 0.57 to 0.93) among OBSP-screened patients.

Patients also had worse overall survival if they were older, lived in a lower-income neighbourhood, had more comorbidities or previous cancer, cancer of a more advanced stage or had triple-negative disease (i.e., negative for the estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2) ($p < 0.0001$ for all, Table 5).

Interpretation

Patients whose breast cancer was screened through the OBSP had a faster time to diagnosis and were more likely to be referred to an O-BAS than symptomatic patients. Attendance at an O-BAS was associated with improved overall survival.

As of 1998, the OBSP implemented a process whereby screened patients can be directly referred for diagnostic follow-up (at an O-BAS or other assessment site) by the OBSP screening site responsible for that patient's workup.[6] Our results show that similar improvements are needed for symptomatic patients (Appendix 1, eFigure S3).[27] Symptomatic patients exhibit features associated with worse prognosis, including older age at diagnosis, more advanced stage at diagnosis and more biologically aggressive tumours.[28–32] The O-BAS are high-volume centres that are equipped to manage complex patients and efficiently render a diagnosis.[6,33] Despite this, symptomatic patients were less likely to be given their diagnosis at an O-BAS (Appendix 1, eFigure S3a-c). A shorter time to treatment may be more important for patients with more aggressive tumours, which appear to be more common among symptomatic patients.[34] However, we observed that symptomatic patients had a longer time until diagnosis (Appendix 1, eFigure S3d-e).[35,36] Anxiety during the diagnostic interval is high, and may be higher for patients with symptoms.[37–39] Thus, symptomatic patients may again derive greater benefit from a shorter diagnostic interval. In addition, since there is comprehensive data collection for the OBSP-screened population, patients who are screened through OBSP can learn about their risk of having cancer, given an abnormal screen. There is no parallel data collection for symptomatic patients who, arguably, may need this information on risk more urgently than asymptomatic patients (Appendix 1, eFigure S3e-g).[40,41]

The OBSP requires that O-BAS adhere to requirements outlined in its standard operating procedures.[22,42] In addition, O-BAS are required to develop mechanisms for ongoing evaluation and quality improvement, and to implement processes to notify the referring physician of abnormal test results, recommendations for biopsy and the diagnosis. However, about 74% of all breast cancer cases are diagnosed outside the OBSP and are therefore not subject to those same standards, reporting and performance management requirements. Funnelling symptomatic patients through an organized system is therefore expected to improve clinical and patient-reported outcomes, and to provide data necessary to inform quality improvement.

Table 3 (part 1 of 2): Factors associated with wait times

Characteristic	Diagnostic interval		Pretreatment interval	
	Adjusted β (95% CI)*	*p* value	Adjusted β (95% CI)*	*p* value
O-BAS				
No	Ref.		Ref.	
Yes	–2.0 (–3.6 to –0.3)		–3.9 (–4.7 to –3.2)	
Screening		< 0.0001		< 0.0001
Symptomatic	Ref.		Ref.	
OBSP-screened	–24.8 (–26.2 to –23.3)		–2.6 (–3.3 to –2.0)	
Non-OBSP-screened	4.7 (3.3 to 6.3)		–1.2 (–1.9 to –0.5)	
Sociodemographic				
Age (per 10-yr increment)	–3.3 (–3.7 to –2.8)		0.3 (0.1 to 0.5)	
Sex				
Female	Ref.		Ref.	
Male	–12.6 (–19.3 to –5.9)		–2.4 (–5.3 to 0.6)	
Neighbourhood income quintile‡		0.97		0.004
Highest	Ref.		Ref.	
Mid-high	–0.4 (–2.2 to 1.4)		0.3 (–0.5 to 1.1)	
Middle	–0.1 (–2.0 to 1.7)		0.6 (–0.2 to 1.4)	
Mid-low	0.2 (–1.7 to 2.0)		1.1 (0.3 to 1.9)	
Lowest	0.2 (–1.7 to 2.2)		1.6 (0.7 to 2.4)	
Neighbourhood immigrant density‡		< 0.0001		0.18
Least dense	Ref.		Ref.	
Mid-dense	3.7 (2.1 to 5.3)		0.4 (–0.3 to 1.1)	
Most dense	6.3 (4.2 to 8.4)		0.9 (–0.1 to 1.9)	
Rurality‡				
Urban	Ref.		Ref.	
Rural	–0.1 (–2.3 to 2.1)		–1.0 (–1.9 to 0.0)	
Distance to closest O-BAS (per 100-km increment)§	0.9 (–3.0 to 4.7)		0.6 (–1.2 to 2.3)	
Clinical				
Charlson Comorbidity Index		< 0.0001		< 0.0001
Missing	–7.8 (–9.1 to –6.5)		1.0 (0.4 to 1.5)	
0	Ref.		Ref.	
1	1.8 (–0.9 to 3.3)		0.4 (–0.5 to 1.4)	
2	–0.5 (–4.2 to 3.1)		1.6 (–0.0 to 3.2)	
≥ 3	–1.8 (–6.0 to 2.4)		5.5 (3.6 to 7.4)	
Previous breast cancer relative to diagnosis, yr		< 0.0001		< 0.0001
Never	Ref.		Ref.	
≤ 5	79.5 (72.4 to 86.6)		–8.2 (–11.5 to –5.0)	
5–10	34.9 (30.9 to 38.9)		0.6 (–1.2 to 2.4)	
≥ 10	12.5 (9.8 to 15.3)		0.5 (–0.8 to 1.7)	
Cancer				
Laterality		0.01		0.22
Right	Ref.		Ref.	
Left	0.3 (–0.9 to 1.5)		–0.3 (–0.9 to 0.2)	
Bilateral	–9.7 (–16.3 to –3.0)		1.6 (–1.4 to 4.6)	

Table 3 (part 2 of 2): Factors associated with wait times

Characteristic	Diagnostic interval		Pretreatment interval	
	Adjusted β (95% CI)*	*p* value	Adjusted β (95% CI)*	*p* value
Cancer stage		< 0.0001		0.0002
0	11.4 (1.8 to 21.0)		7.0 (2.7 to 11.2)	
1	Ref.		Ref.	
2	–9.8 (–11.2 to –8.5)		0.1 (–0.5 to 0.7)	
3	–12.7 (–14.7 to –10.8)		–1.2 (–2.0 to –0.3)	
4	–21.1 (–24.3 to –17.9)		1.0 (–0.3 to 2.4)	
Unknown	8.7 (5.1 to 12.4)		1.5 (–0.2 to 3.2)	
Histology		< 0.0001		< 0.0001
Ductal	Ref.		Ref.	
Lobular	5.4 (3.3 to 7.5)		4.2 (3.3 to 5.1)	
Ductal and lobular	0.9 (–2.0 to 3.7)		4.9 (3.6 to 6.2)	
Adenocarcinoma	6.0 (2.1 to 9.9)		–0.1 (–1.8 to 1.6)	
Mucinous	7.7 (3.4 to 11.9)		–3.8 (–5.7 to –1.9)	
Other	3.8 (1.4 to 6.4)		1.0 (–0.1 to 2.1)	
Hormone receptor profile		0.0007		0.004
ER–, PR–, HER2–	Ref.		Ref.	
ER–, PR–, HER2+	1.4 (–2.0 to 4.8)		–0.7 (–2.2 to 0.8)	
ER–, PR+, HER2–	–1.8 (–10.8 to 7.1)		–1.6 (–5,7 to 2.4)	
ER–, PR+, HER2+	2.3 (–11.6 to 16.3)		0.6 (–5,5 to 6.6)	
ER+, PR–, HER2–	2.7 (–0.3 to 5.7)		–0.3 (–1.6 to 1.1)	
ER+, PR–, HER2+	–1.9 (–6.0 to 2.2)		0.7 (–1.1 to 2.6)	
ER+, PR+, HER2–	–0.1 (–2.3 to 2.0)		1.3 (0.3 to 2.2)	
ER+, PR+, HER+	–1.1 (–4.1 to 1.9)		0.6 (–0.7 to 1.9)	
Missing	3.4 (0.8 to 6.1)		1.4 (0.2 to 2.6)	
Topography		< 0.0001		< 0.0001
Upper-outer quadrant	Ref.		Ref.	
Overlapping lesion	1.9 (0.2 to 3.6)		0.1 (–0.6 to 0.9)	
Breast NOS	9.3 (7.1 to 11.6)		–3.0 (–4.1 to –2.0)	
Lower-outer quadrant	1.0 (–1.1 to 3.1)		0.2 (–0.7 to 1.2)	
Upper-inner quadrant	–0.0 (–1.8 to 1.9)		–0.0 (–0.8 to 0.8)	
Lower-inner quadrant	0.4 (–2.1 to 3.0)		0.2 (–0.7 to 1.2)	
Central portion	3.7 (1.0 to 6.4)		–1.3 (–2.5 to –0.1)	
Nipple	10.6 (6.5 to 14.7)		1.2 (–1.6 to 2.0)	
Axillary tail	1.0 (–6.1 to 8.1)		1.9 (–1.2 to 5.1)	
Other				
Year of diagnosis		< 0.0001		< 0.0001
2013	Ref.		Ref.	
2014	–1.6 (–3.4 to 0.3)		–1.3 (–2.2 to –0.5)	
2015	–3.3 (–5.2 to –1.5)		–2.0 (–2.8 to –1.1)	
2016	–4.2 (–6.0 to –2.3)		–2.2 (–3.0 to –1.4)	
2017	–2.6 (–4.4 to –0.8)		–2.1 (–2.9 to –1.3)	

Note: CI = confidence interval, ER = estrogen receptor, HER2 = human epidermal growth factor receptor-2, NOS = not otherwise specified, O-BAS = OBSP-affiliated breast assessment site, OBSP = Ontario Breast Screening Program, OR = odds ratio, PR = progesterone receptor, Ref. = reference category.
*Diagnostic interval is the time from suspicion of breast cancer until diagnosis (overall mean 62 d, standard deviation [SD] 65.6 d; median 35 d, interquartile range [IQR] 19–82 d). Pre-treatment interval is the time from diagnosis of breast cancer until first treatment (overall mean 38 d, SD 29.5 d; median 34 d, IQR 23–47 d.
†Adjusted for O-BAS status, screening status, age, neighbourhood income quintile, neighbourhood immigrant density, rurality, distance to the closest O-BAS, Charlson Comorbidity Index, previous breast cancer, laterality, cancer stage, hormone receptor profile, topography, year of diagnosis and level of geography (Local Health Integration Network). β coefficients reflect the effect of a 1-unit change in the patient or tumour characteristic on the duration of the time interval, in days.
‡Adapted from Statistics Canada *Postal Code Conversion File* and *Postal Code Conversion File Plus* (June 2017), which is based on data licensed from Canada Post Corporation.[16] We used the patient's postal code at diagnosis.
§β coefficients reflect the effect of a 100-km change in Euclidean distance to the patient's closest O-BAS. We used the patient's postal code at diagnosis.

Table 4: Health care use among patients with breast cancer who were or were not referred to a Breast Assessment Site affiliated with the Ontario Breast Screening Program

	Non-O-BAS		O-BAS	
Type of encounter*	No. (%) of patients *n* = 8862	Days from encounter to diagnosis, median (IQR)†	No. (%) of patients *n* = 42 598	Days from encounter to diagnosis, median (IQR)†
Mammography				
Screening mammography	2683 (30.3)	25 (14 to 41)	18 614 (43.7)	23 (14 to 39)
Diagnostic mammography (first)	6929 (78.2)	14 (3 to 28)	38 708 (90.9)	11 (0 to 23)
Diagnostic mammography (second)	3726 (42.0)	6 (–2 to 20)	25 585 (60.1)	0 (0 to 14)
Diagnostic mammography (third)	1360 (15.3)	0 (–32 to 0)	12 509 (29.4)	0 (–30 to 0)
Any mammography	7386 (83.3)	17 (7 to 34)	40 858 (95.9)	17 (7 to 32)
Other imaging				
Breast ultrasonography (first)	7278 (82.1)	8 (0 to 20)	40 155 (94.3)	5 (0 to 17)
Breast ultrasonography (second)	7114 (80.3)	12 (1 to 23)	39 736 (93.3)	9 (0 to 21)
Breast ultrasonography (third)	3900 (44.0)	0 (0 to 1)	22 379 (52.5)	0 (0)
Abdominal or thoracic ultrasonography	1832 (20.7)	0 (–22 to 43)	8129 (19.1)	–9 (–22 to 47)
Abdominal or thoracic computed tomography	3368 (38.0)	–6 (–22 to 9.5)	10 547 (24.8)	–14 (–25 to 0)
Breast magnetic resonance imaging	1168 (13.2)	–20 (–31 to –9)	9635 (22.6)	–14 (–24 to –5)
Abdominal or thoracic magnetic resonance imaging	1739 (19.6)	–15 (–27 to 2)	11 250 (26.4)	–13 (–23 to 0)
Chest radiography	4300 (48.5)	0 (–21 to 40)	16 738 (39.3)	–11 (–26 to 35)
Biopsy				
Breast biopsy	7543 (85.1)	0 (0 to 0)	41 160 (96.6)	0 (0)
Lymph node biopsy	789 (8.9)	0 (–11 to 0)	3711 (8.7)	0 (–5 to 0)
Any biopsy	7723 (87.1)	0 (0)	41 804 (98.1)	0 (0)
Consultations and visits				
General or general thoracic surgeon	7690 (86.8)	–1 (–14 to 9)	41 300 (97.0)	–8 (–16 to 3)
Cardiac surgery consult	52 (0.6)	53 (–9 to 121)	149 (0.3)	87 (7 to 149)
Dermatology consult	556 (6.3)	86 (22 to 138)	3088 (7.2)	84 (27 to 140)
Cardiology consult	632 (7.1)	55 (0.5 to 128)	2619 (6.1)	63 (–2 to 127)
Primary care provider visit	4337 (48.9)	44 (3 to 115)	17 059 (40.0)	59 (12 to 123)
Medical oncology consult	2310 (26.1)	–22 (–36 to –11)	6180 (14.5)	–19 (–30 to –11)
Internal medicine consult	2131 (24.0)	0 (–18 to 81)	7529 (17.7)	10 (–21 to 104)
Radiation oncology consult	1443 (16.3)	–22 (–36 to –10)	4117 (9.7)	–20 (–33 to –10)
First visit				
Earliest of any of the above until diagnosis	8056 (90.9)	53 (20 to 128)	39 822 (93.5)	49 (19 to 125)
Earliest of any of the above until diagnosis (including diagnosis date)	8862 (100.0)	42 (14 to 121)	42 598 (100.0)	42 (15 to 119)
Suspicion date until diagnosis	7788 (87.9)	39 (20 to 92)	40 052 (94.0)	35 (18 to 79)

Note: IQR = interquartile range, O-BAS = OBSP-affiliated breast assessment site, OBSP = Ontario Breast Screening Program,
*We collected health care encounter and timing of health care encounter relative to the diagnosis date from the Ontario Cancer Registry. We included encounters if they occurred within 6 months before diagnosis until the start of treatment (or 60 days after diagnosis, if no treatment). We identified encounters using billing codes from the Ontario Health Insurance Program, or procedural codes from the Discharge Abstract Database (inpatient) and the National Ambulatory Care Reporting System (outpatient).
†Positive values indicate the encounter occurred before diagnosis; negative values indicate the encounter occurred after diagnosis.

We suspect the existing O-BAS likely have the capacity to evaluate additional patients because most (79%) symptomatic patients in the province were given their diagnoses at an O-BAS (this has increased since the time of writing as more centres have become O-BAS). Although it remains unknown how many symptomatic patients have cancer ruled out at an O-BAS, we suspect this frequency reflects most symptomatic patients in the province because the likelihood of a cancer diagnosis is higher if symptoms are present; the need for a diagnostic biopsy is more likely for symptomatic patients; and O-BAS are more likely to have the ability to perform a biopsy than non-O-BAS.[8,43]

Table 5 (part 1 of 2): Factors associated with all-cause mortality

	Crude		Adjusted	
Factor	HR (95% CI)	*p* value	HR (95% CI)*	*p* value
O-BAS				
No	Ref.		Ref.	
Yes	0.41 (0.39 to 0.43)		0.72 (0.68 to 0.76)	
Screening status		< 0.0001		< 0.0001
Symptomatic	Ref.		Ref.	
OBSP-screened	0.30 (0.27 to 0.33)		0.72 (0.66 to 0.79)	
Non-OBSP-screened	0.43 (0.40 to 0.46)		0.67 (0.62 to 0.72)	
Sociodemographic				
Age (per 10-yr increment)	1.62 (1.59 to 1.65)		1.49 (1.46 to 1.51)	
Sex				
Female	Ref.		Ref.	
Male	2.29 (1.91 to 2.74)		1.43 (1.18 to 1.74)	
Neighbourhood income quintile†		< 0.0001		< 0.0001
Highest	Ref.		Ref.	
Mid-high	1.18 (1.09 to 1.28)		1.13 (1.04 to 1.23)	
Middle	1.29 (1.19 to 1.40)		1.15 (1.06 to 1.25)	
Mid-low	1.45 (1.34 to 1.56)		1.18 (1.09 to 1.28)	
Lowest	1.71 (1.58 to 1.84)		1.29 (1.19 to 1.40)	
Neighbourhood immigrant density†		< 0.0001		< 0.0001
Least dense	Ref.		Ref.	
Mid-dense	0.88 (0.83 to 0.93)		0.97 (0.91 to 1.04)	
Most dense	0.84 (0.79 to 0.90)		0.93 (0.85 to 1.03)	
Rurality†				
Urban	Ref.		Ref.	
Rural	1.09 (1.00 to 1.16)		0.94 (0.86 to 1.03)	
Distance to closest O-BAS (per 100-km increment)‡	1.17 (1.04 to 1.30)		0.90 (0.77 to 1.05)	
Clinical				
Charlson Comorbidity Index		< 0.0001		< 0.0001
Missing	0.73 (0.69 to 0.77)		0.87 (0.82 to 0.92)	
0	Ref.		Ref.	
1	1.75 (1.63 to 1.88)		1.33 (1.23 to 1.44)	
2	2.79 (2.52 to 3.08)		1.66 (1.50 to 1.85)	
≥ 3	4.56 (4.15 to 5.02)		2.55 (2.31 to 2.82)	
Previous breast cancer relative to diagnosis, yr		< 0.0001		< 0.0001
Never	Ref.		Ref.	
≤ 5	2.06 (1.68 to 2.52)		1.65 (1.34 to 2.03)	
5–10	1.55 (1.36 to 1.77)		1.10 (0.95 to 1.26)	
≥ 10	1.39 (1.26 to 1.53)		0.98 (0.88 to 1.08)	
Previous other cancer relative to diagnosis, yr		< 0.0001		< 0.0001
Never	Ref.		Ref.	
≤ 5	2.26 (2.04 to 2.50)		1.63 (1.46 to 1.82)	
5–10	1.72 (1.47 to 2.01)		1.27 (1.08 to 1.49)	
≥ 10	1.74 (1.55 to 1.96)		1.25 (1.11 to 1.42)	

Table 5 (part 2 of 2): Factors associated with all-cause mortality

	Crude		Adjusted	
Factor	HR (95% CI)	*p* value	HR (95% CI)*	*p* value
Cancer				
Laterality		< 0.0001		0.01
Right	Ref.		Ref.	
Left	1.00 (0.95 to 1.05)		0.96 (0.91 to 1.01)	
Bilateral	1.84 (1.50 to 2.27)		1.26 (1.02 to 1.56)	
Cancer stage		< 0.0001		< 0.0001
0	1.31 (0.79 to 2.18)		0.94 (0.55 to 1.61)	
1	Ref.		Ref.	
2	2.12 (1.97 to 2.28)		1.80 (1.66 to 1.94)	
3	4.62 (4.27 to 5.01)		4.10 (3.77 to 4.46)	
4	18.4 (17.0 to 19.9)		13.0 (11.9 to 14.2)	
Unknown	7.68 (6.96 to 8.46)		3.72 (3.30 to 4.19)	
Histology		< 0.0001		< 0.0001
Ductal	Ref.		Ref.	
Lobular	1.13 (1.04 to 1.23)		0.89 (0.82 to 0.98)	
Ductal and lobular	1.03 (0.91 to 1.16)		0.99 (0.88 to 1.13)	
Adenocarcinoma	2.07 (1.84 to 2.33)		0.99 (0.86 to 1.06)	
Mucinous	0.79 (0.64 to 0.97)		0.88 (0.72 to 1.09)	
Other	2.53 (2.26 to 2.71)		1.22 (1.12 to 1.31)	
Hormone receptor profile		< 0.0001		< 0.0001
ER–, PR–, HER2–	Ref.		Ref.	
ER–, PR–, HER2+	0.62 (0.55 to 0.70)		0.50 (0.44 to 0.57)	
ER–, PR+, HER2–	1.07 (0.81 to 1.42)		1.23 (0.93 to 1.63)	
ER–, PR+, HER2+	0.76 (0.47 to 1.23)		0.47 (0.29 to 0.75)	
ER+, PR–, HER2–	0.76 (0.69 to 0.85)		0.62 (0.55 to 0.69)	
ER+, PR–, HER2+	0.64 (0.55 to 0.75)		0.52 (0.44 to 0.61)	
ER+, PR+, HER2–	0.40 (0.37 to 0.43)		0.37 (0.34 to 0.40)	
ER+, PR+, HER2+	0.42 (0.37 to 0.48)		0.39 (0.34 to 0.44)	
Missing	0.95 (0.88 to 1.03)		0.53 (0.48 to 0.58)	
Topography		< 0.0001		< 0.0001
Upper–outer quadrant	Ref.		Ref.	
Overlapping lesion	1.26 (1.18 to 1.36)		1.09 (1.02 to 1.17)	
Breast NOS	2.80 (2.61 to 3.01)		1.41 (1.30 to 1.52)	
Lower–outer quadrant	1.03 (0.94 to 1.14)		1.05 (0.95 to 1.15)	
Upper–inner quadrant	0.90 (0.83 to 0.98)		0.97 (0.89 to 1.06)	
Lower–inner quadrant	1.05 (0.93 to 1.17)		1.02 (0.91 to 1.14)	
Central portion	1.40 (1.26 to 1.55)		1.05 (0.94 to 1.17)	
Nipple	1.28 (1.09 to 1.50)		0.90 (0.76 to 1.06)	
Axillary tail	2.37 (1.91 to 2.93)		1.48 (1.18 to 1.84)	

Note: CI = confidence interval, ER = estrogen receptor, HER2 = human epidermal growth factor receptor-2, HR = hazard ratio, NOS = not otherwise specified, O-BAS = OBSP-affiliated breast assessment site, OBSP = Ontario Breast Screening Program, PR = progesterone receptor, Ref. = reference category.
**n* = 49 383 patients and 6402 events; all estimates are adjusted for O-BAS status, screening status, age, neighbourhood income quintile, neighbourhood immigrant density, rurality, distance to the closest O-BAS, Charlson Comorbidity Index, previous breast cancer, laterality, cancer stage, hormone receptor profile, topography, year of diagnosis and level of geography (Local Health Integration Network).
†Adapted from Statistics Canada *Postal Code Conversion File* and *Postal Code Conversion File Plus* (June 2017), which is based on data licensed from Canada Post Corporation.[16] We used the patient's postal code at diagnosis.
‡Hazard ratios reflect the risk of death for every 100-km increase in Euclidean distance to the patient's closest O-BAS. We used the patient's postal code at diagnosis.

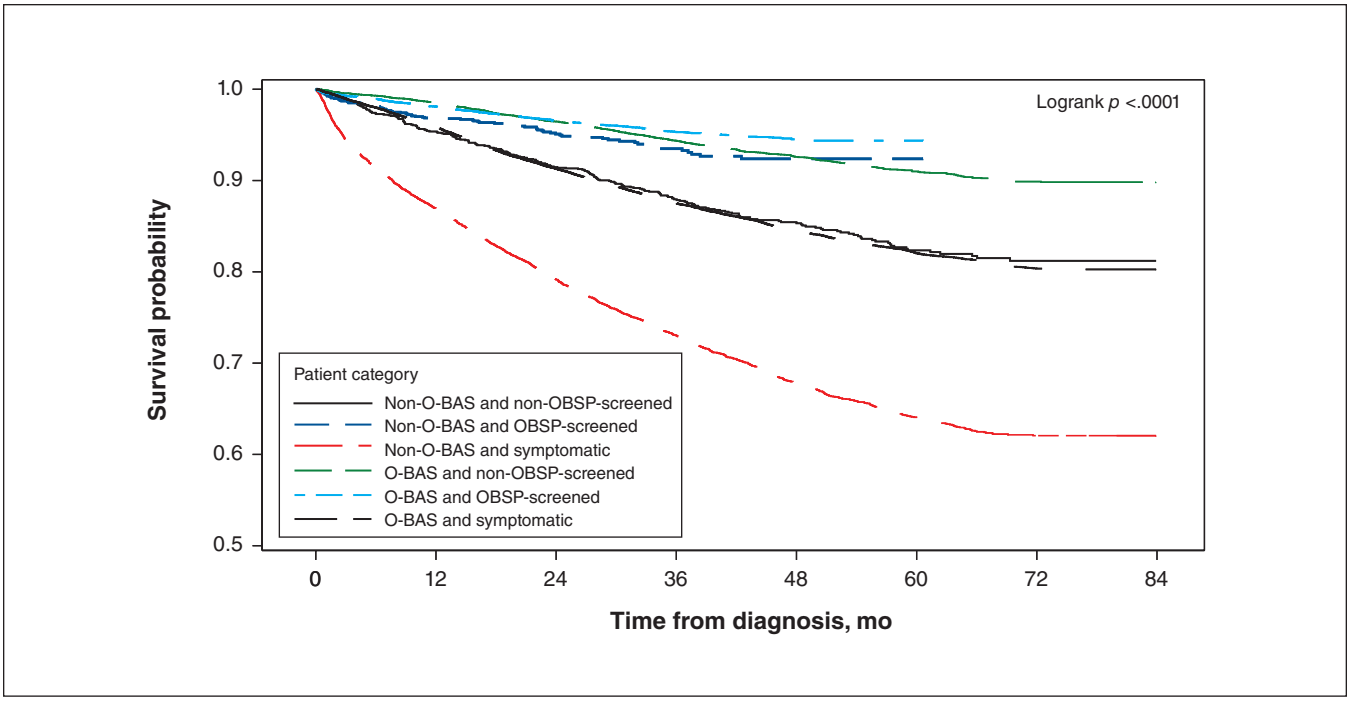

Figure 3: Kaplan–Meier plot for overall survival (by whether the patient's breast cancer was detected by the Ontario Breast Screening Program (OBSP-screened), by screening outside of the OBSP (non-OBSP-screened) or by symptoms and by whether they were referred to an OBSP-affiliated breast assessment site (O-BAS) for diagnosis. We corrected time from diagnosis for lead-time bias.

It remains possible that increased referrals to O-BAS will result in capacity constraints and prolonged wait times. This should be considered when designing system-level changes to the diagnostic process for symptomatic patients. However, a more standardized diagnostic assessment pathway may also reduce repeated imaging and unnecessary testing, which is also expected to reduce costs.[44] A 2018 environmental scan of national and regional cancer diagnostic improvement initiatives described cost savings, but formal cost effectiveness analyses were not available and are warranted.[45]

Limitations

One limitation of this study is the risk of misclassification of non-OBSP-screened cancers (e.g., some may have been symptomatic) and symptomatic cancers (e.g., some may have been incidental, although this is likely uncommon).[46–48] Also, the definition of O-BAS we used is imperfect; it reflects the institution that renders the diagnosis, which may differ from the institution conducting the remainder of the diagnostic workup. Moreover, some institutions function like an O-BAS (e.g., have all the necessary equipment and personnel), but do not have patient navigation or a funding agreement with the OBSP. These centres were classified as non-O-BAS, despite having some O-BAS features.

Patients with previous breast cancers had a significantly longer diagnostic interval than those who did not. However, because the methodology used to identify the suspicion date was developed in a cohort of patients with first-ever breast cancer, it may not be valid in this subgroup of patients.[22,23] Nevertheless, findings from a recent systematic review suggested that patients with a history of breast cancer be included in screening programs (even if not high risk), a conclusion that is supported by our findings.[49]

Hazard ratio estimates of the OBSP-screened group, for which we corrected lead-time bias, assume that the sojourn time (i.e., time for an asymptomatic patient to become symptomatic) of 24 months is accurate.[24] Our results may not generalize to certain patient groups, like men (who are not eligible for OBSP screening) or those with diagnoses of ductal carcinoma in situ (stage 0), which we did not include because it is generally asymptomatic (the few patients classified in our study as stage 0 are likely misclassified).

Finally, our results may not generalize to jurisdictions that do not have organized screening programs or a designated referral stream for symptomatic patients. Although other provinces in Canada have organized screening programs, we are unaware of any provincial-level assessment programs designated for symptomatic patients.[44,50,51] Reviews of the literature related to symptomatic presentation often focus only on wait times as a measure of performance.[52,53]

Conclusion

Patients whose breast cancer was first detected by the OBSP received their diagnoses earlier than symptomatic patients and were more likely to be referred to O-BAS, which was associated with better survival. Our findings suggest that all individuals with signs and symptoms of breast cancer would benefit from organized, high-quality diagnostic assessment processes and standards like those used by the OBSP.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394-424.
2. Ontario Cancer Statistics 2020: Chapter 1 – Estimated current cancer incidence. Toronto: Cancer Care Ontario; 2020. Available: https://www.cancercareontario.ca/en/statistical-reports/ontario-cancer-statistics-2020/ch-1-estimated-current-cancer-incidence (accessed 2020 Nov. 11).
3. Hendrick RE, Helvie MA. Mammography screening: a new estimate of number needed to screen to prevent one breast cancer death. *AJR Am J Roentgenol* 2012;198:723-8.
4. Hendrick RE, Helvie MA. United States Preventive Services Task Force screening mammography recommendations: science ignored. *AJR Am J Roentgenol* 2011;196:W112-6.
5. Webber C, Whitehead M, Eisen A, et al. Breast cancer diagnosis and treatment wait times in specialized diagnostic units compared with usual care: a population-based study. *Curr Oncol* 2020;27:e377-85.
6. Chiarelli AM, Muradali D, Blackmore KM, et al. Evaluating wait times from screening to breast cancer diagnosis among women undergoing organised assessment vs usual care. *Br J Cancer* 2017;116:1254-63.
7. Quan ML, Shumak RS, Majpruz V, et al. Improving work-up of the abnormal mammogram through organized assessment: results from the Ontario breast screening program. *J Oncol Pract* 2012;8:107-12.
8. Koo MM, von Wagner C, Abel GA, et al. Typical and atypical presenting symptoms of breast cancer and their associations with diagnostic intervals: evidence from a national audit of cancer diagnosis. *Cancer Epidemiol* 2017;48:140-6.
9. Jiang L, Gilbert J, Langley H, et al. Breast cancer detection method, diagnostic interval and use of specialized diagnostic assessment units across Ontario, Canada. *Health Promot Chronic Dis Prev Can* 2018;38:358-67.
10. Benchimol EI, Smeeth L, Guttmann A, et al.; RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLoS Med* 2015;12:e1001885.
11. Chiarelli AM, Blackmore KM, Mirea L, et al. Annual vs biennial screening: diagnostic accuracy among concurrent cohorts within the Ontario breast screening program. *J Natl Cancer Inst* 2020;112:400-9.
12. Chiarelli AM, Blackmore KM, Muradali D, et al. Performance measures of magnetic resonance imaging plus mammography in the high risk Ontario breast screening program. *J Natl Cancer Inst* 2020;112:136-44.
13. Ontario Health Insurance Plan. OHIP schedule of benefits and fees. Toronto: Government of Ontario Ministry of Health and Long-Term Care. Available: https://www.health.gov.on.ca/en/pro/programs/ohip/sob/ (accessed 2021 Oct. 18).
14. Canadian Institute for Health Information [home page]. Available: https://www.cihi.ca/en (accessed 2021 Oct. 18).
15. Collaborative Stage data collection system [home page]. Available: http://cancerstaging.org/cstage/Pages/default.aspx (accessed 2021 Oct. 18).
16. Postal Code^{OM} Conversion File Plus (PCCF+). Geographic files and documentation 82F0086X. Ottawa: Statistics Canada. Available: https://www150.statcan.gc.ca/n1/en/catalogue/82F0086X (accessed 2021 Oct. 19).
17. Data catalogue. Toronto: Government of Ontario. Available: https://data.ontario.ca/dataset (accessed 2021 Oct. 18).
18. Jiang L, Gilbert J, Langley H, et al. Is being diagnosed at a dedicated breast assessment unit associated with a reduction in the time to diagnosis for symptomatic breast cancer patients? *Eur J Cancer Care (Engl)* 2018;27:e12864.
19. American Joint Commitee on Cancer. AJCC Cancer *Staging handbook*. Edge S, Byrd DR, Compton CC, et al., editors. New York: Springer New York; 2010:XIX, 718. Available: http://www.springer.com/us/book/9780387884424 (accessed 2021 Oct. 18).
20. Kilgore ML, Smith W, Curtis JR, et al. Evaluating comorbidity scores based on health service expenditures. *Medicare Medicaid Res Rev* 2012;2:mmrr.002.03.a05.
21. Dobbins TA, Creighton N, Currow DC, et al. Look back for the Charlson Index did not improve risk adjustment of cancer surgical outcomes. *J Clin Epidemiol* 2015;68:379-86.
22. Jiang L, Gilbert J, Langley H, et al. Effect of specialized diagnostic assessment units on the time to diagnosis in screen-detected breast cancer patients. *Br J Cancer* 2015;112:1744-50.
23. Groome PA, Webber C, Whitehead M, et al. Determining the cancer diagnostic interval using administrative health care data in a breast cancer cohort. *JCO Clin Cancer Inform* 2019;3:1-10.
24. Duffy SW, Nagtegaal ID, Wallis M, et al. Correcting for lead time and length bias in estimating the effect of screen detection on cancer survival. *Am J Epidemiol* 2008;168:98-104.
25. Land LH, Dalton SO, Jørgensen TL, et al. Comorbidity and survival after early breast cancer. A review. *Crit Rev Oncol Hematol* 2012;81:196-205.
26. Desai AA, Hoskin TL, Day CN, et al. Effect of primary breast tumor location on axillary nodal positivity. *Ann Surg Oncol* 2018;25:3011-8.
27. Raine R, Or Z, Prady S, et al. Essay 5: Evaluating health-care equity. In: Raine R, Fitzpatrick R, Barratt H, et al., editors. *Challenges, Solutions and Future Directions in the Evaluation of Service Innovations in Health Care and Public Health*. Southampton (UK): NIHR Journals Library; 2016.
28. Esserman LJ, Shieh Y, Rutgers EJT, et al. Impact of mammographic screening on the detection of good and poor prognosis breast cancers. *Breast Cancer Res Treat* 2011;130:725-34.
29. Drukker CA, Schmidt MK, Rutgers EJT, et al. Mammographic screening detects low-risk tumor biology breast cancers. *Breast Cancer Res Treat* 2014;144:103-11.
30. Pálka I, Kelemen G, Ormándi K, et al. Tumor characteristics in screen-detected and symptomatic breast cancers. *Pathol Oncol Res* 2008;14:161-7.
31. Lawrence G, Wallis M, Allgood P, et al. Population estimates of survival in women with screen-detected and symptomatic breast cancer taking account of lead time and length bias. *Breast Cancer Res Treat* 2009;116:179-85.
32. Duffy SW, Tabár L, Chen H-H, et al. The impact of organized mammography service screening on breast carcinoma mortality in seven Swedish counties: a collaborative evaluation. *Cancer* 2002;95:458-69.
33. Vrijens F, Stordeur S, Beirens K, et al. Effect of hospital volume on processes of care and 5-year survival after breast cancer: a population-based study on 25000 women. *Breast* 2012;21:261-6.
34. Förnvik D, Lång K, Andersson I, et al. Estimates of breast cancer growth rate from mammograms and its relation to tumour characteristics. *Radiat Prot Dosimetry* 2016;169:151-7.
35. Cox B, Sneyd MJ. Bias in breast cancer research in the screening era. *Breast* 2013;22:1041-5.
36. Caplan L. Delay in breast cancer: implications for stage at diagnosis and survival. *Front Public Health* 2014;2:87.
37. Montgomery M, McCrone SH. Psychological distress associated with the diagnostic phase for suspected breast cancer: systematic review. *J Adv Nurs* 2010;66:2372-90.
38. Murphy PJ, Marlow LAV, Waller J, et al. What is it about a cancer diagnosis that would worry people? A population-based survey of adults in England. *BMC Cancer* 2018;18:86.
39. Balasooriya-Smeekens C, Walter FM, Scott S. The role of emotions in time to presentation for symptoms suggestive of cancer: a systematic literature review of quantitative studies. *Psychooncology* 2015;24:1594-604.
40. Birrell J, Meares K, Wilkinson A, et al. Toward a definition of intolerance of uncertainty: a review of factor analytical studies of the Intolerance of Uncertainty Scale. *Clin Psychol Rev* 2011;31:1198-208.
41. Tan H-J, Marks LS, Hoyt MA, et al. The relationship between intolerance of uncertainty and anxiety in men on active surveillance for prostate cancer. *J Urol* 2016;195:1724-30.
42. Eisen A, Blackmore KM, Meschino WS, et al. Genetic assessment wait time indicators in the High Risk Ontario Breast Screening Program. *Mol Genet Genomic Med* 2018;6:213-23.
43. Singh D, Malila N, Pokhrel A, et al. Association of symptoms and breast cancer in population-based mammography screening in Finland. *Int J Cancer* 2015;136:E630-7.
44. Olivotto IA, Kan L, Mates D, et al. Screening Mammography Program of British Columbia: pattern of use and health care system costs. *CMAJ* 1999;160:337-41.
45. Pollock M, Craig R, Chojecki D, et al. *Initiatives to accelerate the diagnostic phase of cancer care: an environmental scan*. Edmonton: Institute of Health Economics; 2018. Available: https://www.ihe.ca/publications/initiatives-to-accelerate-the-diagnostic-phase-of-cancer-care-an-environmental-scan (accessed 2021 Aug. 28).
46. Healey TT, Agarwal S, Patel R, et al. Cancer yield of incidental breast lesions detected on chest computed tomography. *J Comput Assist Tomogr* 2018;42:453-6.
47. Benveniste AP, Marom EM, Benveniste MF, et al. Incidental primary breast cancer detected on PET-CT. *Breast Cancer Res Treat* 2015;151:261-8.
48. Prabhu V, Chhor CM, Ego-Osuala IO, et al. Frequency and outcomes of incidental breast lesions detected on abdominal MRI over a 7-year period. *AJR Am J Roentgenol* 2017;208:107-13.
49. Muradali D, Kennedy EB, Eisen A, et al. Breast screening for survivors of breast cancer: a systematic review. *Prev Med* 2017;103:70-5.
50. Miller AB, Wall C, Baines CJ, et al. Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. *BMJ* 2014;348:g366.
51. Yuan Y, Vu K, Shen Y, et al. Importance of quality in breast cancer screening practice: a natural experiment in Alberta, Canada. *BMJ Open* 2020;10:e028766.
52. Webber C, Jiang L, Grunfeld E, et al. Identifying predictors of delayed diagnoses in symptomatic breast cancer: a scoping review. *Eur J Cancer Care (Engl)* 2017;26:e12483.
53. Jassem J, Ozmen V, Bacanu F, et al. Delays in diagnosis and treatment of breast cancer: a multinational analysis. *Eur J Public Health* 2014;24:761-7.

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