

The efficiency and effectiveness of breast cancer diagnosis in Ontario: a case for reprioritizing symptomatic patients

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Abstract (words = 250)

Introduction: Most breast cancer patients in Ontario are diagnosed through the Ontario Breast Screening Program (OBSP) and its assessment sites following an abnormal screen or follow-up of symptoms by patients' primary care providers. During the diagnostic evaluation, patients may be referred to an OBSP-affiliated Breast Assessment Site (O-BAS), which includes patient navigators, personnel, and equipment to facilitate a timely and thorough diagnostic evaluation. Unlike OBSP-screened patients, there is no provincial oversight for the diagnostic evaluation of symptomatic patients.

Methods: Patients diagnosed with breast cancer from 2013-2017 were identified from the Ontario Cancer Registry. By linking to other administrative databases, we explored the association of the route to diagnosis (screened or symptomatic) on use of O-BAS, wait times until diagnosis or treatment, healthcare utilization patterns, and overall survival for patients with breast cancer.

Results: 42,598/51,460 (83%) of breast cancer patients were diagnosed at an O-BAS. OBSP-screen-detected patients were more likely than symptomatic patients to be diagnosed at an O-BAS [adjusted odds ratio 1.68 (1.57-1.80)]. O-BAS patients had significantly better overall survival than non-O-BAS patients [adjusted hazard ratio 0.73 (0.66-0.80)]. OBSP-screen-detected patients were diagnosed 1 month quicker than symptomatic patients, but diagnosis at an O-BAS did not affect wait-times.

Conclusion: The efficiency and effectiveness of the OBSP has created a high-quality mechanism for screen-eligible patients to receive timely breast cancer diagnosis and optimal care. Our findings suggest that individuals with signs and symptoms of breast cancer would benefit from the same diagnostic assessment processes and standards employed by the organized screening program.

Introduction

Breast cancer is the second most common malignancy, accounting for 12% of all cancers worldwide.^{1,2} Thus, inefficiencies in care affects many patients and greatly impacts healthcare resources. An international collaborative effort found that patients in Ontario (Canada's largest province) had prolonged wait times for cancer diagnosis compared to select countries.^{3,4} To address this variation, several jurisdictions in Canada and internationally have implemented initiatives to improve the route to cancer diagnosis.⁵

In an effort to improve the timeliness, efficiency, and outcomes of patients undergoing assessment for breast cancer, Ontario Health (Cancer Care Ontario) has designated facilities as Breast Assessment Sites.⁶⁻⁸ To qualify as a Breast Assessment Site, 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.⁶⁻¹⁰ Although these sites are affiliated with the Ontario Breast Screening Program (OBSP), hereby referred to as O-BAS, symptomatic women may also be referred to an O-BAS.

Patients diagnosed with breast cancer typically first engage the healthcare system through their primary care provider with symptomatic presentation or through screening within the OBSP.^{11,12} This initial point of contact is a critical point of divergence for women entering the cancer system. Due to the relationship between the OBSP and O-BAS, we expect fewer symptomatic women to be diagnosed in an O-BAS. Moreover, we expect the diagnostic process to be less efficient for symptomatic women because the patients' general practitioner (GP) coordinates the diagnostic work-up. Regardless of whether a patient is symptomatic or screened, the diagnostic assessment should be efficient and accurate, following best practices and minimizing unnecessary tests.¹³ The time until diagnosis and treatment should also be minimized to reduce patient anxiety during this stressful time.¹⁴

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3 In the present study, we explored the association of the route to diagnosis (screened or
4 symptomatic) on utilization of O-BAS, wait times until diagnosis or treatment, healthcare
5 utilization, and overall survival for patients with breast cancer.
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10 11 12 **Methods**

13 14 15 **Cohort ascertainment**

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18 Adults (age 18+) with an incident invasive breast cancer diagnosed in Ontario between January
19 1, 2013 and December 31, 2017 (ICD-O-3 C50) were identified using the Ontario Cancer
20 Registry (OCR). We included patients who had a valid Ontario health insurance number, an
21 Ontario postal code, and accessed the Ontario Health Insurance Program (OHIP) within 1 year
22 of the diagnosis date. We omitted patients who had a death date before or on the diagnosis
23 date, were diagnosed by autopsy, or had missing age or sex.
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31 32 **Screened versus symptomatic**

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34 Data are collected for all OBSP-screened women through the Integrated Client Management
35 System (ICMS) (**Supplementary Figure S1**). Patients may still be screened outside the
36 auspices of the OBSP, but the patients' GP coordinates the assessment. Patients were
37 classified as "GP-screened" if they had a screening mammogram <12 months prior to diagnosis
38 and were not previously classified as OBSP-screened. The remaining patients were classified
39 as "symptomatic". GP-screened and symptomatic patients may have been screened >12
40 months prior through the OBSP, but this earlier screen did not lead to the present breast cancer
41 diagnosis.
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51 52 **Diagnosis at an O-BAS**

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3 At the time of analysis, there were 72 O-BAS located throughout the province (**Supplementary**
4 **Table S1**). Patients may be assessed at an O-BAS if symptomatic or screened, but the ICMS
5 only collects data on OBSP-screened women. To determine whether GP-screened and
6 symptomatic patients were assessed at an O-BAS, we used the location of the patients' biopsy
7 from billing data, supplemented with the location of the patients' surgery (**Supplementary Table**
8 **S1**).^{12,15}

Healthcare utilization

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19 We explored the frequency and timing of diagnostic tests and consultations or visits with
20 healthcare providers 6 months before diagnosis until the date of first treatment. We searched
21 the OHIP (physician billing) database in addition to the hospital-based databases Discharge
22 Abstract Database (DAD) and the National Ambulatory Care Reporting System (NACRS).
23 Administrative codes are reported in **Supplementary Tables S2-3**.

Diagnostic interval

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33 We defined the diagnostic interval as the time from suspicion of breast cancer until diagnosis
34 from the OCR. For screen-detected cancers, the suspicion date corresponds to the screening
35 mammogram identified from ICMS (OBSP-screened) or OHIP records (GP-screened patients).
36 For symptomatic patients, we searched OHIP, DAD, and NACRS for any relevant diagnostic
37 procedures, consults, visits, and primary care referrals occurring within pre-specified look-back
38 periods using methodology published elsewhere (**Supplementary Tables S4**).^{16,17}

Pre-treatment interval

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49 We defined the pre-treatment interval as the time from diagnosis until treatment started using
50 the earliest of breast resection (Supplementary Table S2), anti-neoplastic systemic therapy, or
51 chest radiation. Antineoplastic therapy was identified from the Activity Level Reporting (ALR)

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3 database, the New Drug Funding Program database, or the Ontario Drug Benefits database,
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5 DAD, or NACRS. Radiation was identified from ALR.
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8 **Other covariates**

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10 We used the Collaborative Staging database to identify overall cancer stage (AJCC 7th edition),
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12 and the tumors' estrogen receptor (ER), progesterone receptor (PR), and human epidermal
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14 growth factor receptor-2 (HER2) status. We used DAD and NACRS to estimate comorbidity
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16 using the Charlson Comorbidity Index with a window of 3 years before the diagnosis date,
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18 excluding cancer (**Supplementary Figure S2**).^{18,19} Sociodemographic characteristics were
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20 derived from the Census using the Postal Code Conversion File+ (version 7B for income and
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22 rurality; version 6C for immigrant density). Health insurance numbers were used for linkage
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24 across databases. All databases employed are used for continuous system performance
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26 monitoring and undergo routine quality checks.
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30 **Statistical methods**

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32 We present means (standard deviation, SD), medians (interquartile range, IQR), and
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34 proportions, where appropriate. We used bivariate or multinomial logistic regression to compare
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36 factors between groups, reporting odds ratios (OR) and 95% confidence intervals (CI). We used
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38 linear regression to explore factors associated with wait-times, reporting beta coefficients and
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40 95% CI, which represent the change in wait times (in days) per unit change in the covariate.
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42 Absence of heteroscedasticity was confirmed using the `autoreg` procedure. We used Cox
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44 proportional hazards regression to explore factors associated with all-cause mortality, reporting
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46 hazard ratios (HR) and 95% CI. Follow-up started at the time of diagnosis and ended at death or
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48 the last known healthcare encounter occurring on or before December 31, 2019. For OBSP-
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50 screen-detected cancer patients, lead-time bias was corrected by subtracting $[1 - \exp(-\lambda t)] / \lambda$ from
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52 the survival time, where λ is the inverse of the mean sojourn time (2 years) and t is the survival
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3 time.²⁰ The date of death was assigned using the OCR, supplemented with the Registered
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5 Persons Database. Unless otherwise stated, all multivariable models were adjusted for O-BAS
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7 status, screened/symptomatic presentation, age, sex, neighbourhood income quintile,
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9 neighbourhood immigrant density, rurality, Charlson comorbidity index, prior breast/non-breast
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11 cancer history, cancer laterality, cancer stage, hormone receptor profile, topography, and
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13 geography (Local Health Integration Network, LHIN). Proportionality was confirmed by visual
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15 inspection of Kaplan-Meier plots, log(-log) survival plots, and Loess-smoothed Schoenfeld
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17 residuals versus time. All analyses were performed using SAS version 9.4 (Cary, NC, SAS
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19 Institute Inc.). Statistical tests were two-sided and evaluated at a 5% significance level. All cells
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21 <6 were suppressed. Ethics approval was not required.
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28 Results

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31 A total 51,460 breast cancer patients were identified (**Supplementary Figure S3**). The mean
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33 age at diagnosis was 63 (SD 13.7) years, 86% had no comorbidity, 3,845 (7%) had a prior
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35 breast cancer and 42,598 (83%) were diagnosed in an O-BAS (**Table 1**). A total 28,107 (55%)
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37 were symptomatic, 13,615 (27%) were OBSP-screened, and 9,738 (19%) were GP-screened.
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40 O-BAS vs. non-O-BAS

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43 After adjustment, O-BAS patients were more likely to be younger, have no comorbidities, live
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45 closer to an O-BAS, and live in a higher-income urban neighbourhood ($p < 0.001$ for all) (**Table**
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47 **1**). O-BAS patients had lower-stage disease ($p < 0.0001$), known hormone receptor status
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49 ($p < 0.0001$), a greater risk of prior breast cancer ($p = 0.0005$), and more likely to have had an
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51 OBSP-screened cancer [OR 1.68 (1.57-1.80)] or GP-screen-detected cancer [OR 1.31 (1.23-
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53 1.41)] than symptomatic.
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OBSP-screened, GP-screened, versus symptomatic

The proportion of patients who were OBSP-screened increased from 23% in 2013 to 29% in 2017 with correspondingly fewer patients presenting with symptoms (**Figure 1**). Symptomatic patients were more likely to reside in a lower-income neighbourhood ($p < 0.0001$), have greater comorbidity ($p < 0.0001$), and have advanced-stage breast cancer than screened patients: 30% of symptomatic patients had stage 1 compared with 47% of GP-screened and 64% of OBSP-screened patients (**Table 2**). Symptomatic patients were more likely to have biologically more aggressive disease: 18% had ER- tumors (versus 11% for OBSP-screened) and 18% had HER2+ tumors (versus 12% for OBSP-screened).

The diagnostic interval

The diagnostic interval was a median 35 (IQR 19, 82) days. Diagnosis at an O-BAS did not reduce the diagnostic interval [beta -2.0 (-3.7, -0.4) days] (**Table 3**) or shorter sub-intervals (e.g. time from suspicion to first image test) (**Supplementary Table S5**). In contrast, compared with stage 1, the diagnostic interval was 10, 12, 21, and 10 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 [beta -10.3 (-17.0, -3.6) days], as did males [beta -13.0 (-19.7, -6.3)]. Compared with symptomatic patients, the diagnostic interval was 25 days shorter [beta -24.8 (-26.3, -23.4)] for OBSP-screened patients and 5 days longer [beta 4.9 (3.3, 6.4) days] for GP-screened patients. No other demographic and clinical factors were meaningfully associated with the length of the diagnostic interval.

The pre-treatment interval

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The first intervention provided was surgery for 40,652 (79%) and systemic therapy for 9,296 (18%) of patients. The pre-treatment interval was a median 34 (IQR 23, 47) days. After adjustment, there were no factors associated with a meaningful delay (**Table 3**).

Healthcare utilization

Frequency: O-BAS patients were more likely to have received various diagnostic tests before treatment than non-O-BAS patients, including a diagnostic mammogram (91% versus 78%), screening mammogram (44% versus 30%), breast biopsy (97% versus 85%), breast ultrasound (94% versus 82%), and breast MRI (23% versus 13%) (**Table 4**). However, O-BAS patients were less likely than non-O-BAS patients to have had an abdominal/thoracic CT scan (25% versus 38%) and a chest x-ray (39% versus 49%). O-BAS patients were more likely than non-O-BAS patients to have a consultation with a general surgeon or general thoracic surgeon (97% versus 87%), but were less likely than non-O-BAS patients to visit their GP (40% versus 49%), have a consultation with an internist (18% versus 24%), or medical oncologist (15% versus 26%).

Timing: O-BAS patients had a consultation or visit with a general surgeon or general thoracic surgeon earlier than non-O-BAS patients (median 8 days versus 1 day before diagnosis) (**Table 4**). The time from diagnosis until consultation with a medical oncologist or radiation oncologist was longer, with a median 20 (11, 32) days and 21 (10, 34) days, respectively.

Overall survival

Patients were followed a mean 42 (SD 21.5) months after diagnosis. After adjustment, patients diagnosed at an O-BAS had better overall survival than non-O-BAS patients [HR 0.73 (0.69-0.78)] (**Table 5**). Overall survival was also better for patients who were either OBSP-screened [HR 0.73 (0.66-0.80)] or GP-screened [HR 0.67 (0.62-0.72)] versus symptomatic. Without

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3 adjustment, O-BAS had a larger impact on survival among symptomatic patients [HR 0.43
4 (0.41-0.45), $p < 0.0001$], and GP-screened patients [HR 0.48 (0.41-0.56), $p < 0.0001$] than OBSP-
5 screened patients [HR 0.69 (0.55-0.88), $p = 0.002$] (p -interaction = 0.0003) (**Figure 2**). In the
6
7 adjusted model, the difference of the effect of O-BAS on overall survival was similar across
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9 patient types (p -interaction=0.80): HR 0.73 (0.69-0.78), $p < 0.0001$ among symptomatic, HR 0.73
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11 (0.62-0.986), $p = 0.0002$ among GP-screened, and HR 0.72 (0.56-0.92), $p = 0.008$ among OBSP-
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13 screened. Patients also had worse overall survival if they were older, lived in a lower-income
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15 neighborhood, had greater comorbidity or prior cancer history, more advanced stage, or triple-
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17 negative disease ($p < 0.0001$ for all) (**Table 5**).
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25 Discussion

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28 In this study, we found that patients screened in an organized program had a faster time until
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30 diagnosis and were more likely to be referred to an O-BAS than symptomatic patients. We also
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32 observed that attendance at an O-BAS was associated with improved overall survival.
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36 As of 1998, the OBSP implemented a process where screened women can be directly
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38 referred for diagnostic follow-up (at an O-BAS or other assessment site) by the OBSP screening
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40 site responsible for that patient's work-up.⁹ The main focus of this system-level change was to
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42 improve the coordination and quality of care for women screened through the OBSP. Our
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44 results demonstrate the success of this program, but similar improvements are needed for
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46 symptomatic patients for several reasons (**Figure 3**).²¹ First, symptomatic patients exhibit
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48 features associated with worse prognosis, including older age at diagnosis, more advanced
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50 stage, and more biologically aggressive tumors.²²⁻²⁶ O-BAS are high-volume centres that are
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52 equipped to manage complex patients and efficiently render a diagnosis.^{9,27} Despite this,
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54 symptomatic patients were less likely to be diagnosed at an O-BAS (**Figure 3, a-c**). Second, a
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3 shorter time until treatment (diagnostic plus pre-treatment intervals) may be important for a
4 subset of patient with more aggressive tumors.²⁸ Patients with fast-growing tumors are less
5 likely to be screen-detected due to length time bias, so any effect of wait times on mortality is
6 expected to be more impactful for symptomatic patients, yet symptomatic patients had a longer
7 time until diagnosis (**Figure 3, d-e**).^{29,30} Third, anxiety during the diagnostic interval is high, and
8 may be higher for patients with symptoms than those without.^{14,31,32} Thus, symptomatic patients
9 may again derive greater benefit from a shorter diagnostic interval. In addition, with
10 comprehensive data collection for the OBSP-screened population, patients can learn about their
11 risk of having cancer given an abnormal screen. There is no parallel for symptomatic patients
12 who, arguably, may need this type of information more urgently than asymptomatic women do
13 (**Figure 3, e-g**).^{33,34}

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27 The OBSP requires that O-BAS adhere to requirements outlined in its standard
28 operating procedures.^{17,35} Additionally, O-BAS are required to develop mechanisms for ongoing
29 evaluation and quality improvement, and to implement processes to notify the referring
30 physician of abnormal test results, recommendations for biopsy, and the diagnosis. However,
31 approximately 74% of all breast cancer cases are diagnosed outside the auspices of the
32 organized screening program and are therefore not subject to those same standards, reporting,
33 and performance management requirements. Funneling symptomatic patients through an
34 organized system is therefore expected to improve clinical and patient-reported outcomes, and
35 provide data necessary to inform quality improvement. We suspect the existing O-BAS likely
36 have the capacity to evaluate these patients because by 2017, 79% of all symptomatic breast
37 cancer patients in the province were diagnosed at an O-BAS (this estimate has increased since
38 the time of writing as more centres have become O-BAS). While it remains unknown how many
39 symptomatic patients without breast cancer are assessed at an O-BAS, we suspect that O-BAS
40 are also ruling-out cancer in many of these patients because: 1) the likelihood of a cancer

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3 diagnosis is higher if symptoms are present; 2) the need for a diagnostic biopsy is more likely
4 for symptomatic patients; and 3) O-BAS are more likely to have the ability to perform a biopsy
5 than non-O-BAS.^{11,36} It remains possible that increased referrals to O-BAS will result in capacity
6 constraints and prolonged wait-times. This should be considered when designing system-level
7 changes to the diagnostic process for symptomatic women. However, a more standardized
8 diagnostic assessment pathway may also reduce repeated imaging and unnecessary testing,
9 which is also expected to reduce costs.³⁷ A 2018 environmental scan of national and regional
10 cancer diagnostic improvement initiatives described cost savings, but formal cost effectiveness
11 analyses were not available.⁵ Such analyses should be considered prior to full implementation
12 of O-BAS.
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25 One limitation of this study is the risk of misclassification of GP-screened cancers (e.g.
26 some may have been symptomatic) and symptomatic cancers (e.g. some may have been
27 incidental findings). However, the demographic, clinical, and tumor characteristics of the GP-
28 screened group was in-between that of the OBSP-screened and symptomatic groups,
29 suggesting that this misclassification is small. Further, the rate of incidental breast cancer
30 detection is believed to be low.^{38–40} Second, the gold standard definition of O-BAS is imperfect:
31 it reflects the institution that renders the diagnosis, which may differ from the institution
32 conducting the remainder of the diagnostic work-up. Also, there are some institutions that
33 function like an O-BAS (e.g. have all the necessary equipment and personnel), but they do not
34 have patient navigation or a funding agreement with the OBSP. These centres were classified
35 as non-O-BAS, despite having some O-BAS features. Third, patients with prior breast cancers
36 had a significantly longer diagnostic interval than those who did not. However, because the
37 suspicion algorithm was developed in a cohort of first-ever breast cancer patients, it may not be
38 valid in this subgroup of patients.^{16,17} Nevertheless, findings from a recent systematic review
39 recommend that patients with a prior history of breast cancer be included in screening programs
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(even if not high-risk), a conclusion that is supported by our findings.⁴¹ Fourth, information on sociodemographic factors were limited to neighbourhood-level classification rather than individual-level, which may result in misclassification on estimates of income and immigrant density. Fifth, our results may not generalize to certain patient groups, like males. Further, our results may not generalize to patients who are diagnosed with ductal carcinoma *in situ*, which was out-of-scope in the present analysis because it is generally asymptomatic. The small number of patients classified as stage 0 are likely misclassified. Finally, our results may not generalize to other jurisdictions that do not have organized screening programs or have a designated referral stream for symptomatic women. While other provinces in Canada have organized screening programs, we are unaware of any provincial-level assessment programs designated for symptomatic women.^{37,42,43} Reviews of the literature related to symptomatic presentation often focus only on wait-times as a measure of performance.^{44,45}

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 employed by the OBSP. There is a clear need to extend provincial oversight and performance monitoring for all individuals undergoing breast assessment for a possible cancer diagnosis.

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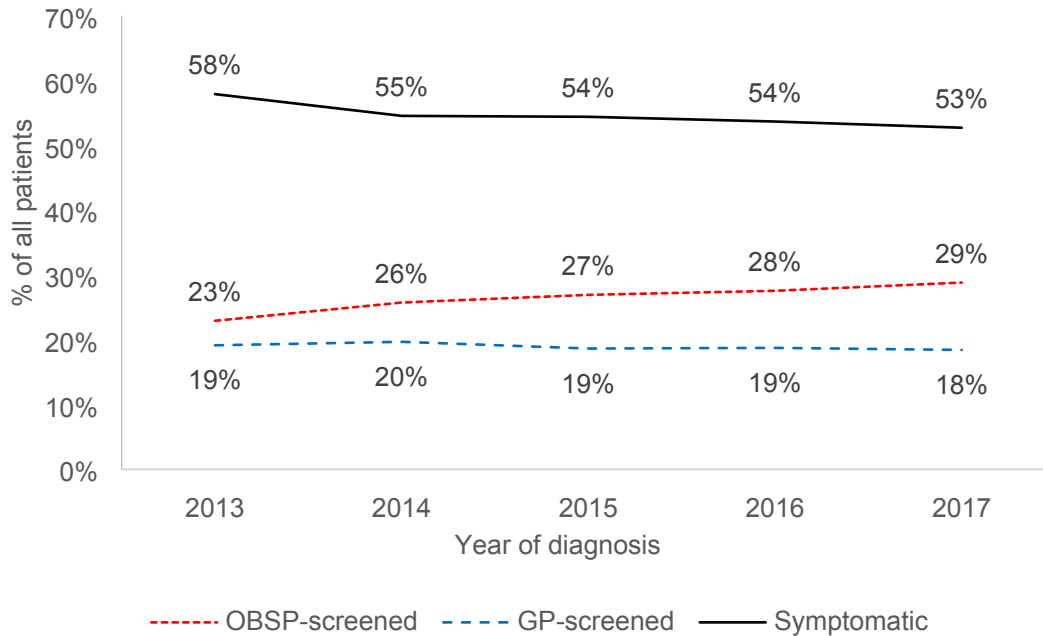
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Optimizing care for symptomatic breast cancer patients

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Figure 1: Change in the proportion of patients screened over time

A) All patients



B) Subgroup of presumed OBSP-eligible patients (females aged 50-74 with no prior breast cancer history)

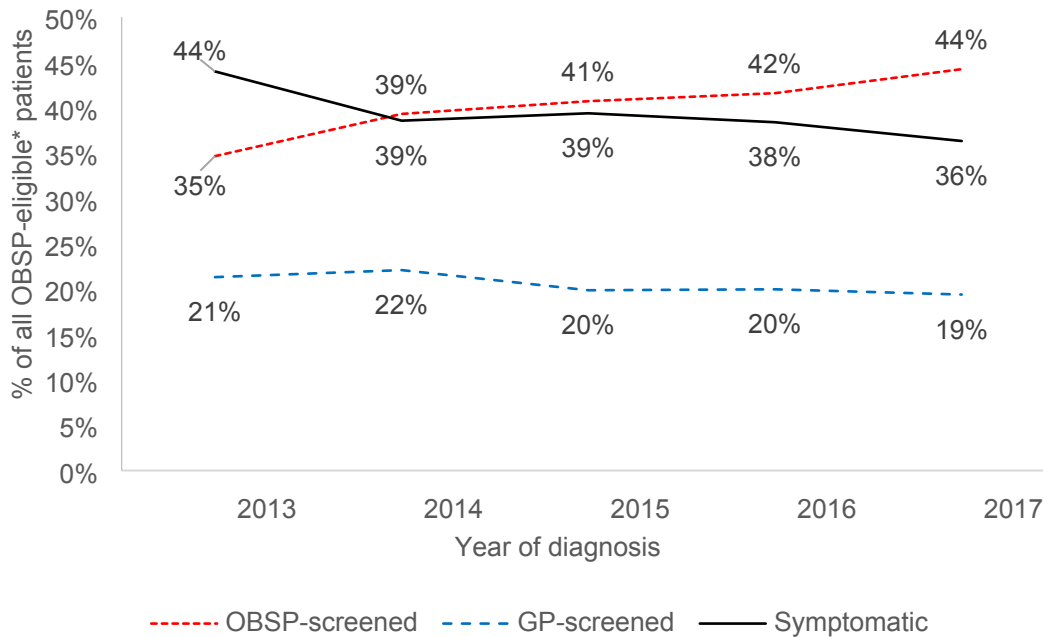
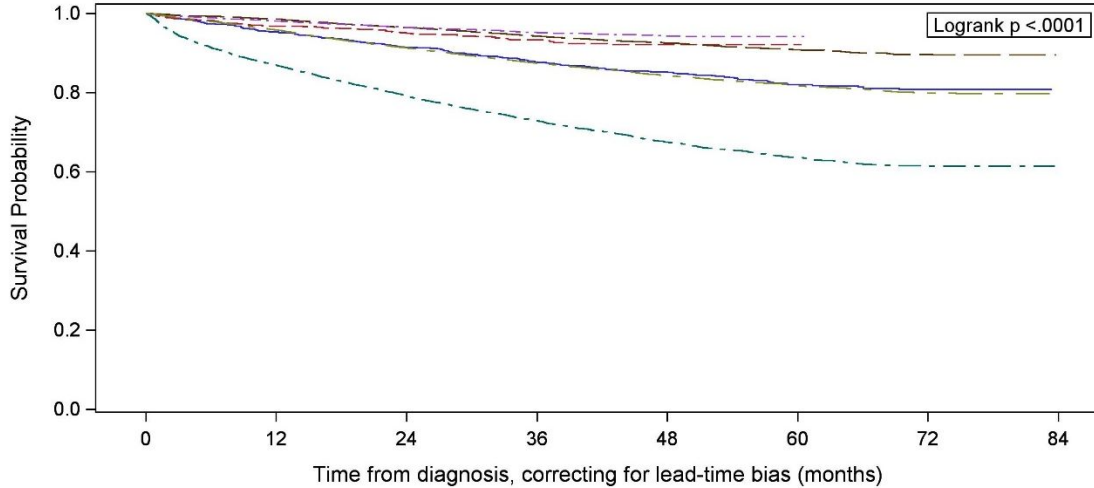


Figure 2: Kaplan-Meier plot for overall survival by screening and O-BAS

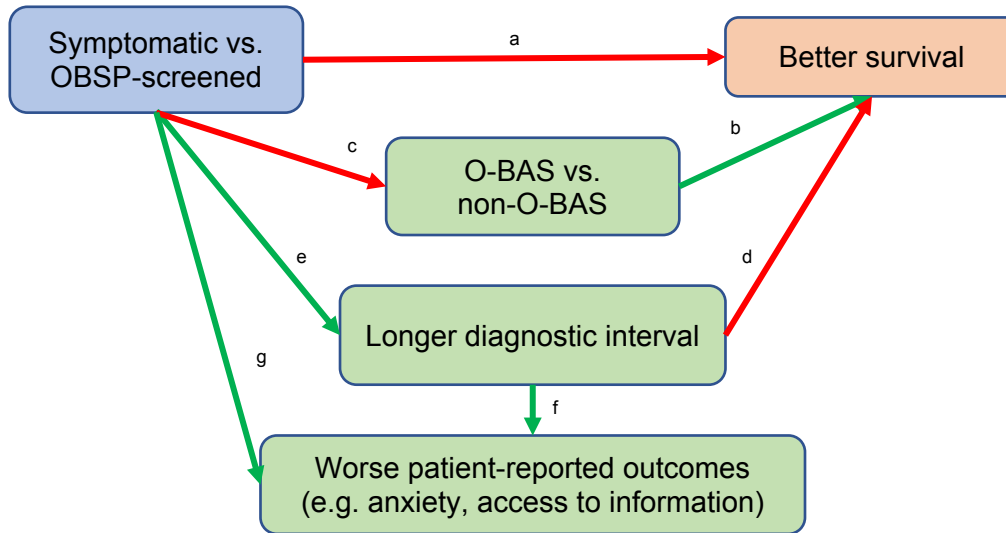


Patient category	
1: Non-O-BAS/GP-screened	2: Non-O-BAS/OBSP-screened
3: Non-O-BAS/symptomatic	4: O-BAS/GP-screened
5: O-BAS/OBSP-screened	6: O-BAS/symptomatic

1	1475	1394	1317	997	698	442	199	0
2	1476	1243	786	462	215	2	0	0
3	5897	5090	4538	3314	2223	1376	593	0
4	8255	8089	7764	5967	4287	2714	1185	0
5	12138	10451	6964	4238	1795	19	0	0
6	22180	21127	19708	14722	10370	6451	2893	0

Kaplan-Meier plot for overall survival by whether patients were diagnosed at an O-BAS and whether they were OBSP-screened-detected, screened by their GP (general practitioner) or symptomatic. OBSP – Ontario Breast Screening Program; O-BAS – OBSP-affiliated breast assessment site

Figure 3: Causal diagram of symptomatic versus screened patients



^a symptomatic patients have features (e.g. demographic, clinical, and tumor characteristics) that negatively affect survival

^b O-BAS is associated with better overall survival

^c symptomatic patients are less likely to be referred to an O-BAS

^d a longer diagnostic interval may result in worse survival for some patients

^e symptomatic patients have a longer diagnostic interval

^f a longer diagnostic interval may increase patient anxiety and other patient-reported outcomes

^g symptomatic patients are more likely to have anxiety due to the presence of painful or noticeable breast symptoms, independent of wait-times

O-BAS - breast assessment site affiliated with the Ontario Breast Screening Program

Table 1: Comparison of socio-demographic, clinical factors and tumor characteristics between O-BAS and non-O-BAS breast cancer patients

	Non-O-BAS N=8862	O-BAS N=42598	O-BAS vs. non-O-BAS (crude)		O-BAS vs. non-O-BAS (adjusted) ^a	
			OR (95% CI)	p-value	OR (95% CI)	p-value
Screening status						
Symptomatic	5908 (67%)	22199 (52%)	1.0 (ref)	<.0001	1.0 (ref)	<.0001
GP-screened	1477 (17%)	8261 (19%)	1.49 (1.40-1.58)		1.31 (1.23-1.41)	
OBSP-screened	1477 (17%)	12138 (29%)	2.19 (2.06-2.33)		1.68 (1.57-1.80)	
Patient socio-demographic factors						
Sex						
Female	8750 (98.7%)	42285 (99.3%)	1.0 (ref)	<.0001	1.0 (ref)	0.58
Male	112 (1.3%)	313 (0.7%)	0.58 (0.47-0.72)		0.93 (0.73-1.19)	
Age (x10) years						
<50	66 (SD 14.6)	63 (SD 13.5)	0.87 (0.85-0.88)	<.0001	0.88 (0.86-0.90)	<.0001
50-74	1328 (15%)	7244 (17%)	1.0 (ref)	<.0001	–	–
>74	4833 (55%)	26048 (61%)	0.99 (0.93-1.06)			
	2701 (30%)	9306 (22%)	0.63 (0.59-0.68)			
After-tax neighbourhood income quintile ^b						
Highest	1756 (20%)	9368 (22%)	1.0 (ref)	<.0001	1.0 (ref)	<.0001
Mid-high	1640 (19%)	8235 (20%)	0.94 (0.88-1.01)		0.91 (0.84-0.99)	
Middle	1678 (19%)	8291 (20%)	0.93 (0.86-1.00)		0.93 (0.85-1.00)	
Mid-low	1797 (20%)	8539 (20%)	0.89 (0.83-0.96)		0.88 (0.81-0.95)	
Lowest	1933 (22%)	7695 (18%)	0.75 (0.70-0.80)		0.77 (0.70-0.83)	
Neighbourhood immigrant density ^b						
Least dense	5221 (59%)	24537 (58%)	1.0 (ref)	0.004	1.0 (ref)	0.0002
Mid-dense	2068 (24%)	10661 (25%)	1.10 (1.04-1.16)		1.08 (1.01-1.16)	
Most dense	1497 (17%)	7061 (17%)	1.00 (0.94-1.07)		0.91 (0.83-1.00)	
Rurality ^b						
Urban	7479 (85%)	37789 (90%)	1.0 (ref)	<.0001	1.0 (ref)	<.0001
Rural	1326 (15%)	4351 (10%)	0.65 (0.61-0.69)		0.65 (0.59-0.71)	
Distance (per 100km) ^c						
	15.7±21.6	11.9±19.2	0.44 (0.40- 0.49)	<.0001	0.36 (0.31-0.42)	<.0001
Patient clinical factors						
Charlson Comorbidity index						
Missing	3011 (34%)	16228 (38%)	1.12 (1.06-1.18)		1.04 (0.98-1.10)	
0	4318 (49%)	20825 (49%)	1.0 (ref)	<.0001	1.0 (ref)	0.0002
1	935 (10%)	3665 (9%)	0.81 (0.75-0.88)		0.89 (0.81-0.97)	
2	316 (4%)	1088 (2%)	0.71 (0.63-0.81)		0.88 (0.76-1.02)	
3+	282 (3%)	792 (2%)	0.58 (0.51-0.67)		0.78 (0.66-0.91)	
Prior breast cancer history relative to index diagnosis ^d						
Never	8074 (91%)	39541 (93%)	1.0 (ref)	<.0001	1.0 (ref)	
≤5 years	72 (1%)	250 (1%)	0.71 (0.55-0.92)		1.04 (0.78-1.39)	0.0005
5-10 years	239 (3%)	852 (2%)	0.73 (0.63-0.84)		1.21 (1.02-1.42)	

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≥10 years	477 (5%)	1955 (5%)	0.84 (0.76-0.93)		1.25 (1.11-1.41)	
Prior non-breast cancer history relative to index diagnosis						
Never	8180 (92%)	39563 (93%)	1.0 (ref)	<.0001	1.0 (ref)	0.14
≤5 years	295 (3%)	1172 (3%)	0.82 (0.72-0.94)		1.00 (0.86-1.15)	
5-10 years	136 (2%)	686 (2%)	1.04 (0.87-1.26)		1.22 (1.00-1.50)	
≥10 years	251 (3%)	1177 (3%)	0.97 (0.84-1.11)		1.11 (0.95-1.29)	

Cancer characteristics

Laterality						
Right	4288 (48%)	20701 (49%)	1.0 (ref)	0.47	1.0 (ref)	0.02
Left	4329 (49%)	21516 (51%)	1.03 (0.98-1.08)		1.03 (0.97-1.08)	
Bilateral	65 (1%)	319 (1%)	1.02 (0.78-1.33)		1.49 (1.11-2.01)	
Cancer stage						
0	28 (<1%)	171 (<1%)	0.91 (0.61-1.36)		1.46 (0.95-2.24)	
1	2755 (32%)	18463 (44%)	1.0 (ref)	<.0001	1.0 (ref)	<.0001
2	2861 (33%)	15707 (38%)	0.82 (0.77-0.87)		0.91 (0.85-0.97)	
3	1134 (13%)	5023 (12%)	0.66 (0.61-0.71)		0.75 (0.69-0.82)	
4	1085 (12%)	1343 (3%)	0.19 (0.17-0.20)		0.23 (0.21-0.26)	
Unknown	832 (10%)	1167 (3%)	0.21 (0.19-0.23)		0.36 (0.31-0.40)	
Hormone receptor profile						
ER-, PR-, HER2-	679 (10%)	3814 (10%)	1.0 (ref)	0.08	1.0 (ref)	<.0001
ER-, PR-, HER2+	325 (5%)	1807 (5%)	0.99 (0.86-1.14)		1.04 (0.89-1.21)	
ER-, PR+, HER2-	36 (1%)	182 (0%)	0.90 (0.62-1.30)		1.11 (0.75-1.64)	
ER-, PR+, HER2+	20 (0%)	69 (0%)	0.61 (0.37-1.02)		0.91 (0.53-1.58)	
ER+, PR-, HER2-	561 (8%)	2751 (8%)	0.87 (0.77-0.99)		0.89 (0.78-1.01)	
ER+, PR-, HER2+	204 (3%)	1036 (3%)	0.90 (0.76-1.07)		0.96 (0.80-1.16)	
ER+, PR+, HER2-	4379 (66%)	24116 (66%)	0.98 (0.90-1.07)		0.93 (0.84-1.02)	
ER+, PR+, HER2+	473 (7%)	2773 (8%)	1.04 (0.92-1.19)		0.99 (0.87-1.14)	
Missing	2185	6050	0.49 (0.45-0.54)		0.67 (0.60-0.75)	
Topography						
Upper-outer quadrant	2754 (31%)	15672 (37%)	1.0 (ref)	<.0001	1.0 (ref)	<.0001
Breast NOS	1452 (16%)	3411 (8%)	0.41 (0.38-0.44)		0.69 (0.63-0.75)	
Overlapping lesion	1618 (18%)	7720 (18%)	0.84 (0.78-0.90)		0.93 (0.86-1.00)	
Upper-inner quadrant	1007 (11%)	5806 (14%)	1.01 (0.94-1.10)		0.98 (0.90-1.07)	
Lower-outer quadrant	721 (8%)	4056 (10%)	0.99 (0.90-1.08)		1.00 (0.91-1.10)	
Central portion	503 (6%)	2205 (5%)	0.77 (0.69-0.86)		0.92 (0.83-1.03)	
Lower-inner quadrant	470 (5%)	2558 (6%)	0.96 (0.86-1.06)		0.98 (0.87-1.09)	
Nipple	236 (3%)	922 (2%)	0.69 (0.59-0.80)		0.76 (0.65-0.90)	
Axillary tail	101 (1%)	248 (0.1%)	0.43 (0.34-0.55)		0.55 (0.43-0.72)	

Other characteristics

Year of diagnosis (row percentages provided)						
2013	1767 (18%)	8037 (82%)	1.0 (ref)	0.01	1.0 (ref)	0.03
2014	1748 (17%)	8447 (83%)	1.06 (0.99-1.14)		1.02 (0.95-1.11)	
2015	1715 (17%)	8518 (83%)	1.09 (1.02-1.18)		1.03 (0.95-1.12)	
2016	1882 (18%)	8695 (82%)	1.02 (0.95-1.09)		0.97 (0.90-1.05)	
2017	1750 (16%)	8901 (84%)	1.12 (1.04-1.20)		1.10 (1.02-1.19)	

^a N=49,420; adjusted for screening status, age, neighbourhood income quintile, neighbourhood immigrant density, rurality, distance to the closest O-BAS, Charlson comorbidity index, prior breast cancer history, prior non-breast cancer history, laterality, cancer stage, hormone receptor profile, topography, year of diagnosis and level of geography (Local Health Integration Network, LHIN).

^b source: (or 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. The patients' postal code at diagnosis was used.

^c odds ratio reflects the odds of being diagnosed in a O-BAS for every 100-kilometer increase in Euclidean distance to the patients' closest O-BAS. The patients' postal code at diagnosis was used.

^d numbers rounded to nearest tenth to prevent back-calculation of small cells

OR – odds ratio; CI – confidence interval; OBSP – Ontario Breast Screening Program; O-BAS – OBSP-affiliated Breast Assessment Site; GP – general practitioner; ER – estrogen receptor; PR – progesterone receptor; HER2 – human epidermal growth factor receptor-2; NOS – not otherwise specified

Confidential

Table 2: Comparison of socio-demographic, clinical and cancer characteristics between screened and symptomatic breast cancer patients

	OBSP- screened N=13615 (26%)	GP- screened N=9738 (19%)	Symptomatic N=28107 (55%)	OBSP-screen- detected OR (95% CI)^a	GP-screened OR (95% CI)^a	p-value^a
O-BAS						
Yes	12138 (89%)	8261 (85%)	22199 (79%)	1.73 (1.62-1.86)	1.26 (1.18-1.35)	<.0001
No	1477 (11%)	1477 (15%)	5908 (21%)	1.0 (ref)	1.0 (ref)	
Patient socio-demographic characteristics						
Sex						
Female	13615 (100)	9714 (99.8)	27706 (98.6)	N/A	0.18 (0.12-0.28)	<.0001
Male	0 (0.0)	24 (0.3)	401 (1.4)	N/A	1.0 (ref)	
Age (continuous)	63.7±8.0	62.1±12.2	63.4±16.1	1.09 (0.07-1.11)	0.96 (0.94-0.98)	<.0001
Neighbourhood income quintile ^b						
Highest	3042 (23%)	2243 (23%)	5839 (21%)	1.0 (ref)	1.0 (ref)	<.0001
Mid-high	2727 (20%)	1943 (20%)	5205 (19%)	1.05 (0.98-1.12)	0.97 (0.90-1.04)	
Middle	2707 (20%)	1870 (19%)	5392 (19%)	1.03 (0.96-1.10)	0.91 (0.84-0.98)	
Mid-low	2703 (20%)	1913 (20%)	5720 (21%)	0.98 (0.91-1.05)	0.86 (0.80-0.93)	
Lowest	2275 (17%)	1667 (17%)	5686 (20%)	0.85 (0.79-0.92)	0.76 (0.71-0.83)	
Neighbourhood immigrant density ^b						
Least dense	8368 (62%)	5068 (52%)	16322 (58%)	1.0 (ref)	1.0 (ref)	<.0001
Mid-dense	3124 (23%)	2704 (28%)	6901 (25%)	0.92 (0.86-0.97)	1.21 (1.14-1.28)	
Most dense	2018 (15%)	1897 (20%)	4643 (17%)	0.96 (0.89-1.03)	1.38 (1.28-1.48)	
Rurality ^b						
Urban	11765 (87%)	8790 (91%)	24713 (89%)	1.0 (ref)	1.0 (ref)	0.004
Rural	1693 (13%)	848 (9%)	3136 (11%)	1.13 (1.04-1.23)	0.97 (0.88-1.07)	
Distance to closest O-BAS (km) ^c	13.2±20.2	10.8±14.9	12.8±20.8	1.00 (0.87-1.15)	0.72 (0.61-0.85)	0.0005
Patient clinical characteristics						
Charlson Comorbidity Index						
Missing	5328 (39%)	3839 (39%)	10072 (36%)	1.07 (1.02-1.13)	1.05 (1.00-1.11)	
0	6738 (49%)	4784 (49%)	13621 (48%)	1.0 (ref)	1.0 (ref)	<.0001
1	1095 (8%)	778 (8%)	2727 (10%)	0.84 (0.77-0.91)	0.89 (0.81-0.98)	
2	277 (2%)	185 (2%)	942 (3%)	0.66 (0.56-0.77)	0.63 (0.53-0.74)	
3+	177 (1%)	152 (2%)	745 (3%)	0.53 (0.44-0.63)	0.70 (0.58-0.84)	
Prior breast cancer history relative to index diagnosis						
Never	13576 (100%)	8693 (89%)	25346 (90%)	1.0 (ref)	1.0 (ref)	<.0001
≤5 years	<6	83 (1%)	235 (1%)	0.03 (0.01-0.08)	0.91 (0.70-1.18)	

5-10 years	17 (<1%)	293 (3%)	785 (3%)	0.03 (0.02-0.05)	1.02 (0.88-1.17)	
≥10 years	22 (<1%)	669 (7%)	1741 (6%)	0.02 (0.01-0.03)	1.05 (0.95-1.15)	
Prior non-breast cancer history relative to index diagnosis						
Never	12718 (93%)	9096 (93%)	25929 (92%)	1.0 (ref)	1.0 (ref)	<.0001
≤5 years	313 (2%)	269 (3%)	885 (3%)	0.62 (0.54-0.72)	0.96 (0.83-1.11)	
5-10 years	221 (2%)	149 (2%)	452 (2%)	0.86 (0.72-1.03)	1.04 (0.86-1.27)	
≥10 years	363 (3%)	224 (2%)	841 (3%)	0.72 (0.63-0.82)	0.80 (0.68-0.94)	

Cancer characteristics

Laterality						
Right	6660 (49%)	4735 (49%)	13594 (49%)	1.0 (ref)	1.0 (ref)	0.01
Left	6881 (51%)	4909 (51%)	14055 (50%)	0.99 (0.95-1.04)	1.00 (0.96-1.05)	
Bilateral	71 (<1%)	61 (<1%)	252 (1%)	0.61 (0.46-0.81)	0.75 (0.56-1.00)	
Cancer stage						
0	32 (<1%)	62 (1%)	105 (<1%)	0.38 (0.25-0.57)	0.99 (0.71-1.38)	
1	8523 (64%)	4529 (47%)	8166 (30%)	1.0 (ref)	1.0 (ref)	<.0001
2	3859 (29%)	3235 (34%)	11474 (42%)	0.31 (0.29-0.32)	0.51 (0.48-0.54)	
3	731 (5%)	1057 (11%)	4369 (16%)	0.16 (0.15-0.18)	0.44 (0.40-0.47)	
4	97 (1%)	269 (3%)	2062 (7%)	0.06 (0.05-0.07)	0.26 (0.22-0.29)	
Unknown	185 (1%)	405 (4%)	1409 (5%)	0.25 (0.21-0.30)	0.56 (0.49-0.65)	
Hormone receptor profile						
ER-, PR-, HER2-	895 (7%)	822 (8%)	2776 (10%)	1.0 (ref)	1.0 (ref)	<.0001
ER-, PR-, HER2+	402 (3%)	394 (4%)	1336 (5%)	1.00 (0.87-1.16)	1.01 (0.88-1.17)	
ER-, PR+, HER2-	29 (<1%)	45 (<1%)	144 (1%)	0.64 (0.41-0.98)	1.08 (0.76-1.53)	
ER-, PR+, HER2+	11 (<1%)	15 (<1%)	63 (<1%)	0.79 (0.40-1.56)	0.97 (0.55-1.74)	
ER+, PR-, HER2-	923 (7%)	625 (6%)	1764 (6%)	1.53 (1.36-1.72)	1.18 (1.04-1.33)	
ER+, PR-, HER2+	274 (2%)	222 (2%)	744 (3%)	1.21 (1.02-1.43)	1.03 (0.87-1.23)	
ER+, PR+, HER2-	8736 (64%)	5347 (55%)	14412 (51%)	1.51 (1.39-1.65)	1.14 (1.05-1.25)	
ER+, PR+, HER2+	742 (5%)	575 (6%)	1929 (7%)	1.19 (1.06-1.35)	1.00 (0.88-1.13)	
Missing	1603 (12%)	1693 (17%)	4939 (18%)	1.20 (1.07-1.34)	1.22 (1.09-1.35)	
Topography						
Upper-outer quadrant	5462 (40%)	3497 (36%)	9467 (34%)	1.0 (ref)	1.0 (ref)	<.0001
Overlapping lesion	2578 (19%)	1742 (18%)	5018 (18%)	0.91 (0.86-0.97)	0.97 (0.91-1.04)	
Breast NOS	811 (6%)	876 (9%)	3176 (11%)	0.61 (0.56-0.68)	0.84 (0.77-0.92)	
Lower-outer quadrant	1227 (9%)	948 (10%)	2602 (9%)	0.81 (0.74-0.88)	0.98 (0.90-1.07)	
Upper-inner quadrant	1986 (15%)	1260 (13%)	3567 (13%)	0.85 (0.79-0.91)	0.90 (0.83-0.97)	
Lower-inner quadrant	820 (6%)	578 (6%)	1630 (6%)	0.83 (0.75-0.91)	0.92 (0.83-1.03)	
Central portion	477 (4%)	539 (6%)	1692 (6%)	0.62 (0.55-0.69)	1.00 (0.90-1.12)	
Nipple	202 (1%)	233 (2%)	723 (3%)	0.55 (0.46-0.65)	0.88 (0.75-1.04)	
Axillary tail	52 (<1%)	65 (<1%)	232 (<1%)	0.54 (0.39-0.76)	0.87 (0.65-1.16)	

Other characteristics

Year of diagnosis (row percent provided)						
2013	2248 (23%)	1877 (19%)	5679 (58%)	1.0 (ref)	1.0 (ref)	<.0001
2014	2625 (26%)	2007 (20%)	5563 (55%)	1.17 (1.09-1.26)	1.10 (1.02-1.18)	
2015	2756 (27%)	1908 (19%)	5569 (54%)	1.24 (1.15-1.34)	1.04 (0.97-1.13)	
2016	2915 (28%)	1983 (19%)	5679 (54%)	1.29 (1.20-1.39)	1.07 (0.99-1.15)	
2017	3071 (29%)	1963 (18%)	5617 (53%)	1.40 (1.31-1.51)	1.07 (0.99-1.15)	

^a N=49,420; derived from a multinomial logistic regression adjusted for all variables in the table. All odds ratios (OR) and 95% confidence intervals (CI) use symptomatic as the referent.

^b source: (or 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. The patients' postal code at diagnosis was used.

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° average Euclidean distance to the patients' closest O-BAS. The patients' postal code at diagnosis was used.
OBSP – Ontario Breast Screening Program; O-BAS – OBSP-affiliated Breast Assessment Site; GP – general practitioner; ER –
estrogen receptor; PR – progesterone receptor; HER2 – human epidermal growth factor receptor-2; NOS – not otherwise
specified; N/A – not applicable

Confidential

Table 3: Factors associated with wait-times

	Diagnostic interval (time from suspicion until diagnosis)		Pre-treatment interval (time from diagnosis until first treatment)	
	N=46,004 Mean 62 (SD 65.6) days Median 35 (IQR 19, 82) days		N=48,316 Mean 38 (SD 29.5) days Median 34 (IQR 23, 47) days	
	Adjusted beta (95% CI) ^a	p-value	Adjusted beta (95% CI) ^a	p-value
O-BAS				
No	0 (ref)	0.01	0 (ref)	<.0001
Yes	-2.0 (-3.7, -0.4)		-3.9 (-4.6, -3.2)	
Screening				
Symptomatic	0 (ref)	<.0001	0 (ref)	<.0001
OBSP-screened	-24.8 (-26.3, -23.4)		-2.6 (-3.2, -1.9)	
GP-screened	4.9 (3.3, 6.4)		-1.1 (-1.8, -0.4)	
Patient socio-demographic characteristics				
Age (continuous)	-3.1 (-3.6, -2.7)	<.0001	0.4 (0.2, 0.6)	0.0003
Male sex	-13.0 (-19.7, -6.3)	0.0001	-2.9 (-5.8, 0.1)	0.06
Neighbourhood income quintile^b				
Highest	0 (ref)		0 (ref)	0.006
Mid-high	-0.4 (-2.2, 1.4)		0.3 (-0.5, 1.1)	
Middle	-0.1 (-2.0, 1.7)		0.5 (-0.3, 1.4)	
Mid-low	0.1 (-1.7, 2.0)		1.1 (0.2, 1.9)	
Lowest	0.2 (-1.7, 2.2)	0.98	1.5 (0.6, 2.4)	
Neighbourhood immigrant density^b				
Least dense	0 (ref)	<.0001	0 (ref)	0.24
Mid-dense	3.8 (2.2, 5.3)		0.4 (-.4, 1.1)	
Most dense	6.3 (4.2, 8.5)		0.8 (-0.1, 1.8)	
Rurality^b				
Urban	0 (ref)	0.92	0 (ref)	0.05
Rural	-0.1 (-2.3, 2.1)		-1.0 (-2.0, -0.0)	
Distance to closest O-BAS, per 100km ^c	0.8 (-3.1, 4.7)	0.68	0.5 (-1.2, 2.2)	0.56
Patient clinical characteristics				
Charlson Comorbidity Index				
Missing	-7.8 (-9.1, -6.6)		1.0 (0.4, 1.5)	
0	0 (ref)	<.0001	0 (ref)	<.0001
1	1.1 (-1.0, 3.3)		0.4 (-0.6, 1.3)	
2	-0.6 (-4.3, 3.0)		1.6 (-0.1, 3.2)	
3+	-1.9 (-6.1, 2.3)		5.5 (3.6, 7.4)	
Prior breast cancer history relative to index diagnosis				
Never	0 (ref)	<.0001	0 (ref)	<.0001
≤5 years	79.9 (72.8, 87.0)		-8.2 (-11.4, -4.9)	
5-10 years	35.0 (31.1, 39.0)		0.8 (-1.1, 2.6)	

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≥10 years	12.5 (9.7, 15.3)		0.7 (-0.6, 1.9)	
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Cancer characteristics

Laterality

Right	0 (ref)	0.007	0 (ref)	0.27
Left	0.3 (-0.8, 1.5)		-0.3 (-0.8, 0.2)	
Bilateral	-10.3 (-17.0, -3.6)		1.4 (-1.5, 4.4)	

Cancer stage

0	13.5 (4.0, 23.0)		7.5 (3.2, 11.7)	
1	0 (ref)	<.0001	0 (ref)	0.0002
2	-9.6 (-10.9, -8.3)		0.4 (-0.2, 1.0)	
3	-12.3 (-14.3, -10.4)		-0.5 (-1.4, 0.3)	
4	-20.5 (-23.7, -17.3)		1.5 (0.1, 2.9)	
Unknown	9.8 (6.2, 13.4)		1.8 (0.2, 3.5)	

Hormone receptor profile

ER-, PR-, HER2-	1.0 (ref)	0.002	0 (ref)	<.0001
ER-, PR-, HER2+	1.1 (-2.3, 4.5)		-0.8 (-2.3, 0.7)	
ER-, PR+, HER2-	-2.2 (-11.1, 6.7)		-1.7 (-5.7, 2.3)	
ER-, PR+, HER2+	1.9 (-12.1, 15.9)		0.4 (-5.7, 6.5)	
ER+, PR-, HER2-	3.2 (0.2, 6.1)		0.4 (-0.9, 1.7)	
ER+, PR-, HER2+	-2.4 (-6.5, 1.8)		0.7 (-1.1, 2.6)	
ER+, PR+, HER2-	0.1 (-1.9, 2.2)		1.8 (0.8, 2.7)	
ER+, PR+, HER2+	-1.5 (-4.5, 1.5)		0.8 (-0.6, 2.0)	
Missing	3.7 (1.1, 6.4)		1.8 (0.6, 3.0)	

Topography

Upper-outer quadrant	0 (ref)	<.0001	0 (ref)	<.0001
Overlapping lesion	1.9 (0.3, 3.6)		0.1 (-0.6, 0.8)	
Breast NOS	9.7 (7.4, 11.9)		-3.1 (-4.2, -2.1)	
Lower-outer quadrant	1.0 (-1.1, 3.1)		0.2 (-0.8, 1.1)	
Upper-inner quadrant	-0.0 (-1.9, 1.8)		-0.1 (-0.9, 0.7)	
Lower-inner quadrant	0.3 (-2.2, 2.9)		0.0 (-1.1, 1.2)	
Central portion	3.7 (1.0, 6.4)		-1.3 (-2.5, -0.1)	
Nipple	10.8 (6.7, 14.9)		0.2 (-1.6, 2.0)	
Axillary tail	1.2 (-5.9, 8.3)		1.9 (-1.3, 5.1)	

Other characteristics

Year of diagnosis

2013	0 (ref)	0.0001	0 (ref)	<.0001
2014	-1.6 (-3.4, 0.3)		-1.3 (-2.2, -0.5)	
2015	-3.3 (-5.2, -1.5)		-2.0 (-2.9, -1.2)	
2016	-4.1 (-6.0, -2.3)		-2.2 (-3.0, -1.4)	
2017	-2.6 (-4.4, -0.7)		-2.1 (-2.9, -1.3)	

Beta coefficients reflect the effect of a 1-unit change in the patient/tumour characteristic on the duration of the time interval, in days.

^a adjusted for O-BAS, screening status, age, neighbourhood income quintile, neighbourhood immigrant density, rurality, distance to the closest O-BAS, Charlson comorbidity index, prior breast cancer history, laterality, cancer stage, hormone receptor profile, topography, year of diagnosis and level of geography (Local Health Integration Network, LHIN).

^b source: (or 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. The patients' postal code at diagnosis was used.

OR – odds ratio; CI – confidence interval; OBSP – Ontario Breast Screening Program; O-BAS – OBSP-affiliated Breast Assessment Site; GP – general practitioner; ER – estrogen receptor; PR – progesterone receptor; HER2 – human epidermal growth factor receptor-2; NOS – not otherwise specified

Table 4: Healthcare utilization among non-O-BAS and O-BAS patients

Type of encounter ^a	Non-O-BAS (N=8,862)		O-BAS (N=42,598)	
	N (%)	Median (IQR) days until diagnosis ^b	N (%)	Median (IQR) days until diagnosis ^b
Mammography				
Screening mammogram	2683 (30%)	25 (14, 41)	18614 (44%)	23 (14, 39)
Diagnostic mammogram (first)	6929 (78%)	14 (3, 28)	38708 (91%)	11 (0, 23)
Diagnostic mammogram (second)	3726 (42%)	6 (-2, 20)	25585 (60%)	0 (0, 14)
Diagnostic mammogram (third)	1360 (15%)	0 (-32, 0)	12509 (29%)	0 (-30, 0)
Any mammogram	7386 (83%)	17 (7, 34)	40858 (96%)	17 (7, 32)
Other imaging				
Breast ultrasound (first)	7278 (82%)	8 (0, 20)	40155 (94%)	5 (0, 17)
Breast ultrasound (second)	7114 (80%)	12 (1, 23)	39736 (93%)	9 (0, 21)
Breast ultrasound (third)	3900 (44%)	0 (0, 1)	22379 (53%)	0 (0, 0)
Abdominal/thoracic ultrasound	1832 (21%)	0 (-22, 43)	8129 (19%)	-9 (-22, 47)
Abdominal/thoracic computed tomography scan	3368 (38%)	-6 (-22, 9.5)	10547 (25%)	-14 (-25, 0)
Breast magnetic resonance imaging scan	1168 (13%)	-20 (-31, -9)	9635 (23%)	-14 (-24, -5)
Abdominal/thoracic magnetic resonance imaging scan	1739 (20%)	-15 (-27, 2)	11250 (26%)	-13 (-23, 0)
Chest x-ray	4300 (49%)	0 (-21, 40)	16738 (39%)	-11 (-26, 35)
Biopsy				
Breast biopsy	7543 (85%)	0 (0, 0)	41160 (97%)	0 (0, 0)
Lymph node biopsy	789 (9%)	0 (-11, 0)	3711 (9%)	0 (-5, 0)
Any biopsy	7723 (87%)	0 (0, 0)	41804 (98%)	0 (0, 0)
Consultations and visits				
General or general thoracic surgeon	7690 (87%)	-1 (-14, 9)	41300 (97%)	-8 (-16, 3)
Cardiac surgery consult	52 (<1%)	53 (-9, 121)	149 (<1%)	87 (7, 149)
Dermatology consult	556 (6%)	86 (22, 138)	3088 (7%)	84 (27, 140)
Cardiology consult	632 (7%)	55 (0.5, 128)	2619 (6%)	63 (-2, 127)
General practitioner visit	4337 (49%)	44 (3, 115)	17059 (40%)	59 (12, 123)
Medical oncology consult	2310 (26%)	-22 (-36, -11)	6180 (15%)	-19 (-30, -11)
Internal medicine consult	2131 (24%)	0 (-18, 81)	7529 (18%)	10 (-21, 104)
Radiation oncology consult	1443 (16%)	-22 (-36, -10)	4117 (10%)	-20 (-33, -10)
First visit				
Earliest of any of the above until diagnosis	8056 (91%)	53 (20, 128)	39822 (94%)	49 (19, 125)
Earliest of any of the above until diagnosis (including diagnosis date)	8862 (100%)	42 (14, 121)	42598 (100%)	42 (15, 119)
Suspicion date until diagnosis	7788 (88%)	39 (20, 92)	40052 (94%)	35 (18, 79)

Healthcare encounter and timing of healthcare encounter relative to the diagnosis date from the Ontario Cancer Registry.

Encounters were included if they occurred within 6 months before diagnosis until the start of treatment (or 60 days after diagnosis if no treatment), inclusive

^a encounters were identified 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)

^b positive values indicate the encounter occurred before diagnosis; negative values indicate the encounter occurred after diagnosis

IQR – interquartile range (25th, 75th percentile)

Table 5: Factors associated with all-cause mortality

	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)^a	p-value
O-BAS				
No	1.0 (ref)	<.0001	1.0 (ref)	<.0001
Yes	0.41 (0.39-0.43)		0.73 (0.69-0.78)	
Screening status				
Symptomatic	1.0 (ref)	<.0001	1.0 (ref)	<.0001
OBSP-screened	0.30 (0.27-0.33)		0.73 (0.66-0.80)	
GP-screened	0.43 (0.40-0.46)		0.67 (0.62-0.72)	
Patient socio-demographic characteristics				
Age (continuous)	1.62 (1.59- 1.65)	<.0001	1.48 (1.45-1.51)	<.0001
Male sex	2.29 (1.91- 2.74)	<.0001	1.50 (1.24-1.82)	<.0001
Neighbourhood income quintile ^b				
Highest	1.0 (ref)	<.0001	1.0 (ref)	<.0001
Mid-high	1.18 (1.09-1.28)		1.15 (1.06-1.25)	
Middle	1.29 (1.19-1.40)		1.18 (1.09-1.29)	
Mid-low	1.45 (1.34-1.56)		1.22 (1.12-1.32)	
Lowest	1.71 (1.58-1.84)		1.35 (1.25-1.46)	
Neighbourhood immigrant density ^b				
Least dense	1.0 (ref)	<.0001	1.0 (ref)	<.0001
Mid-dense	0.88 (0.83-0.93)		0.92 (0.85-0.96)	
Most dense	0.84 (0.79-0.90)		0.82 (0.76-0.89)	
Rurality ^b				
Urban	1.0 (ref)	0.04	1.0 (ref)	0.46
Rural	1.09 (1.00-1.16)		0.97 (0.89-1.06)	
Distance to closest O-BAS, per 100km	1.17 (1.04-1.30)	0.008	0.92 (0.79-1.07)	0.26
Patient clinical characteristics				
Charlson comorbidity index				
Missing	0.73 (0.69-0.77)		0.87 (0.82-0.92)	
0	1.0 (ref)	<.0001	1.0 (ref)	<.0001
1	1.75 (1.63-1.88)		1.33 (1.24-1.44)	
2	2.79 (2.52-3.08)		1.66 (1.50-1.85)	
3+	4.56 (4.15-5.02)		2.54 (2.30-2.81)	
Prior breast cancer history relative to index diagnosis				
Never	1.0 (ref)	<.0001	1.0 (ref)	<.0001
≥10 years prior	1.39 (1.26-1.53)		0.97 (0.88-1.08)	
5-10 years prior	1.55 (1.36-1.77)		1.09 (0.95-1.26)	
≤5 years prior	2.06 (1.68-2.52)		1.62 (1.32-1.99)	
Prior non-breast cancer history relative to index diagnosis				
Never	1.0 (ref)	<.0001	1.0 (ref)	<.0001
≥10 years prior	1.74 (1.55-1.96)		1.26 (1.11-1.42)	
5-10 years prior	1.72 (1.47-2.01)		1.26 (1.08-1.48)	
≤5 years prior	2.26 (2.04-2.50)		1.61 (1.45-1.81)	
Cancer characteristics				

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3	Laterality				
4	Right	1.0 (ref)	<.0001	1.0 (ref)	0.01
5	Left	1.00 (0.95-1.05)		0.96 (0.91-1.01)	
6	Bilateral	1.84 (1.50-2.27)		1.28 (1.04-1.59)	
7					
8	Cancer stage				
9	0	1.31 (0.79-2.18)		1.02 (0.60-1.75)	
10	1	1.0 (ref)	<.0001	1.0 (ref)	<.0001
11	2	2.12 (1.97-2.28)		1.79 (1.66-1.94)	
12	3	4.62 (4.27-5.01)		4.08 (3.75-4.43)	
13	4	18.4 (17.0-19.9)		13.1 (12.0-14.2)	
14	Unknown	7.68 (6.96-8.46)		3.77 (3.35-4.24)	
15	Hormone receptor profile				
16	ER-, PR-, HER2-	1.0 (ref)	<.0001	1.0 (ref)	<.0001
17	ER-, PR-, HER2+	0.62 (0.55-0.70)		0.49 (0.43-0.56)	
18	ER-, PR+, HER2-	1.07 (0.81-1.42)		1.23 (0.93-1.63)	
19	ER-, PR+, HER2+	0.76 (0.47-1.23)		0.46 (0.28-0.74)	
20	ER+, PR-, HER2-	0.76 (0.69-0.85)		0.59 (0.53-0.65)	
21	ER+, PR-, HER2+	0.64 (0.55-0.75)		0.51 (0.43-0.60)	
22	ER+, PR+, HER2-	0.40 (0.37-0.43)		0.35 (0.33-0.39)	
23	ER+, PR+, HER2+	0.42 (0.37-0.48)		0.38 (0.34-0.43)	
24	Missing	0.95 (0.88-1.03)		0.53 (0.49-0.58)	
25	Topography				
26	Upper-outer quadrant	1.0 (ref)	<.0001	1.0 (ref)	<.0001
27	Overlapping lesion	1.26 (1.18-1.36)		1.09 (1.02-1.18)	
28	Breast NOS	2.80 (2.61-3.01)		1.39 (1.29-1.50)	
29	Lower-outer quadrant	1.03 (0.94-1.14)		1.05 (0.95-1.15)	
30	Upper-inner quadrant	0.90 (0.83-0.98)		0.96 (0.88-1.06)	
31	Lower-inner quadrant	1.05 (0.93-1.17)		1.03 (0.92-1.16)	
32	Central portion	1.40 (1.26-1.55)		1.04 (0.93-1.15)	
33	Nipple	1.28 (1.09-1.50)		0.91 (0.77-1.08)	
34	Axillary tail	2.37 (1.91-2.93)		1.47 (1.18-1.83)	

^a N=49,383 and 6402 events, all estimates are adjusted for O-BAS, screening status, age, neighbourhood income quintile, neighbourhood immigrant density, rurality, distance to the closest O-BAS, Charlson comorbidity index, prior breast cancer history, laterality, cancer stage, hormone receptor profile, topography, and year of diagnosis

^b source: (or 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. The patients' postal code at diagnosis was used.

HR – hazard ratio; CI – confidence interval; OBSP – Ontario Breast Screening Program; O-BAS – OBSP-affiliated Breast Assessment Site; GP – general practitioner; ER – estrogen receptor; PR – progesterone receptor; HER2 – human epidermal growth factor receptor-2; NOS – not otherwise specified

The efficiency and effectiveness of breast cancer diagnosis in Ontario: a case for reprioritizing symptomatic patients

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Abstract (words = 250)

Introduction: Most breast ~~ct-cancers~~ patients in Ontario are diagnosed through the Ontario Breast Screening Program (OBSP) ~~and its assessment sites~~ following an abnormal screen or follow-up of symptoms by ~~a~~ patients' primary care providers. During the diagnostic evaluation, patients may be referred to an OBSP-affiliated Breast Assessment Site (O-BAS), which includes patient navigators, ~~and necessary~~ personnel, and equipment to facilitate a timely and thorough diagnostic evaluation. Unlike OBSP-screened patients, there is no provincial oversight for the diagnostic evaluation of symptomatic patients.

Methods: Patients diagnosed with breast cancer from 2013-2017 were identified from the Ontario Cancer Registry. ~~By linking to other administrative databases, we explored the association of the route to diagnosis (screened or symptomatic) on referral use of to O-BAS, wait times until diagnosis or treatment, healthcare utilization patterns, and overall survival for patients with breast cancer. We assessed the effect of diagnosis at an O-BAS and presentation with symptoms on wait-times, patterns of healthcare utilization, and overall survival.~~

Results: ~~42,598/Of the~~ 51,460 (83%) of breast cancer patients identified, 83% were diagnosed at an O-BAS. OBSP-screen-detected patients were ~~significantly~~ more likely than symptomatic patients to be diagnosed at an O-BAS [adjusted odds ratio ~~1.68 (1.57-1.80)~~ 1.61 (1.49-1.74)]. O-BAS patients had significantly better overall survival than non-O-BAS patients [adjusted hazard ratio ~~0.73 (0.66-0.80)~~ 0.74 (0.69-0.80)]. OBSP-screen-detected patients were diagnosed 1 month quicker than symptomatic patients, but diagnosis at an O-BAS did not affect wait-times. ~~A longer interval between diagnosis and treatment was associated with better overall survival.~~

Conclusion: The efficiency and effectiveness of the OBSP has created a high-quality mechanism for screen-eligible patients to receive ~~a~~ timely breast cancer diagnosis and optimal care. Our findings suggest that individuals with signs and symptoms of breast cancer would benefit from the ~~organized- same~~ diagnostic assessment processes and standards employed by the ~~OBSP~~ organized screening program.

Introduction

Breast cancer is the second most common malignancy, accounting for 12% of all cancers worldwide.^{1,2} Thus, inefficiencies in care affects many patients and greatly impacts healthcare resources. An international collaborative effort found that patients in Ontario (Canada's largest province) had prolonged wait times for cancer diagnosis compared to select countries.^{3,4} To address this variation, several jurisdictions in Canada and internationally have implemented initiatives to improve the route to cancer diagnosis.⁵

In an effort to improve the timeliness, efficiency, and outcomes of patients undergoing breast screening assessment for breast cancer, the Ontario Ministry of Health has supported Ontario Health (Cancer Care Ontario), which is responsible for the OBSP, to has designated facilities as OBSP-affiliated Breast Assessment Sites (O-BAS).⁶⁻⁸ To qualify as a Breast Assessment Site O-BAS, 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.⁶⁻¹⁰ Although these sites are affiliated with the Ontario Breast Screening Program (OBSP), hereby referred to as O-BAS, symptomatic women may also be referred to an O-BAS.

Pppatients diagnosed with breast cancer typically first engaged the healthcare system either through their primary care provider with symptomatic presentation of breast symptoms (most commonly a breast lump) or through screening mammography within received a screening test through the Ontario Breast Screening Program (OBSP).^{11,12} This initial point of contact is a critical point of divergence for women entering the cancer system. Due to the relationship between the OBSP and O-BAS, we expect fewer symptomatic women to be diagnosed in an O-BAS. Moreover, we expect the diagnostic process to be less efficient for

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3 symptomatic women because the patients' general practitioner (GP) coordinates the diagnostic
4 work-up.

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8 Regardless of whether a patient ~~was is~~ symptomatic or screened, ~~diagnostic~~
9 ~~assessment should be sensitive (such that all cancers are identified) and specific (to avoid~~
10 ~~overdiagnosis and overtreatment).~~ ~~The the~~ diagnostic assessment should ~~also~~ be efficient and
11 accurate, following best practices and minimizing unnecessary tests.¹³ ~~Further, t~~The time until
12 diagnosis and treatment ~~should also be minimized to reduce is fraught with patient~~ anxiety for
13 ~~the patient and during this stressful time~~ should be minimized whenever possible.¹⁴ However,
14 there is little evidence that shorter wait times result in improved clinical outcomes.^{7,8}

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23 ~~To improve the timeliness, efficiency, and outcomes of patients undergoing breast~~
24 ~~screening, the Ontario Ministry of Health has supported Ontario Health (Cancer Care Ontario),~~
25 ~~which is responsible for the OBSP, to designate OBSP-affiliated Breast Assessment Sites (O-~~
26 ~~BAS).~~⁹⁻¹⁴ ~~To qualify as an O-BAS, facilities are required to have a patient navigation system that~~
27 ~~coordinates referrals through a defined clinical pathway and have access to diagnostic imaging,~~
28 ~~image-guided biopsies, pathology, and surgical services.~~ In the present study, we explored the
29 association of ~~O-BAS and~~ the route to diagnosis (screened or symptomatic) on referral
30 utilization of O-BAS, wait times until diagnosis or treatment, referral rates to O-BAS,
31 healthcare utilization, and overall survival for patients with breast cancer.

Methods

Cohort ascertainment

Adults (age 18+) with an incident invasive breast cancer diagnosis in Ontario between January 1, 2013 and December 31, 2017 (ICD-O-3 ~~topography code C50; ICD-O-D behavior code = 3~~) were identified using the Ontario Cancer Registry (OCR). We ~~restricted the cohort to~~ included patients ~~with who had~~ a valid Ontario health-insurance card number, an Ontario postal code, and ~~patients who accessed the healthcare system through~~ the Ontario Health Insurance Program (OHIP) within 1 year of the diagnosis date. We ~~also~~ omitted patients who had a death date before or on the diagnosis date, were diagnosed by autopsy, or had missing age or sex.

~~Classifying patients as S~~screened versus ~~and~~ symptomatic

~~The OBSP has operated since 1990 to deliver organized, population-based breast screening to eligible women ages 50-74.¹⁰ Women are ineligible if they had a prior breast cancer, augmentation mammoplasty, or if they currently have acute breast symptoms. Although most women are screened biennially, those at increased breast cancer risk are screened annually. The OBSP was expanded in July 2011 to screen women age 30 to 69 years at high risk for breast cancer with annual digital mammography and MRI or screening breast ultrasound if MRI is contraindicated.¹¹ Women who meet at least one of the high-risk criteria are eligible even if they have a prior history of breast and/or other cancers, breast implants, or had a unilateral mastectomy.~~

~~The OBSP sites typically coordinate the diagnostic work-up for women with an abnormal screen (typically a mammogram) until cancer is diagnosed or ruled-out. The patients' general practitioner (GP) is apprised of the screening results, and in many cases is not required to make referrals for diagnostic tests. Data are collected for all OBSP-screened women through the Integrated Client Management System (ICMS), a database that is managed at Ontario Health~~

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(Cancer Care Ontario). To identify OBSP-screened women, the ICMS was used (Supplementary Figure S1). Patients may still be screened outside the auspices of the OBSP. This may include patients who are OBSP-ineligible (e.g. due to age), or receive interval screens (e.g. between the screening dates recommended by the OBSP). For these patients, but the patients' their GP coordinates the screening and assessment/ diagnostic processes. We therefore refer to these patients as "GP-screened". Patients were classified as "GP-screened" if they had a screening mammogram (OHIP billing codes X172 or X178) within ≤ 12 months prior to diagnosis and were not previously classified as OBSP-screened. The remaining patients were classified as "symptomatic", acknowledging that some of these may have been incidental asymptomatic cases. GP-screened and symptomatic patients may have been screened >12 months prior through the OBSP, but this earlier screening was not the one that did not lead to result in a the present breast cancer diagnosis.

Classifying patients as diagnosed at an O-BAS and non-OBAS

At the time of analysis, there were 72 O-BAS located throughout the province (Supplementary Table S1). Ontario facilities that provide organized assessment must have certified mammography technologists and equipment that meets or exceeds that specified by Canadian Association of Radiologist's Mammography Accreditation Program (CAR-MAP); provide all abnormal mammographic work-up, including special mammographic views and image-guided core biopsy; provide radiological, surgical and pathologic consultation with experts in breast evaluation; and provide navigation for patient support and coordination of referrals. O-BAS may either perform all the required services for abnormal mammographic work-up, or establish networks with facilities to provide the services.^{10,11}

Patients may can be assessed at an O-BAS if symptomatic or screened, regardless of whether they were OBSP-screened, GP-screened, or symptomatic. However, but to support data collection O-BAS are remunerated by the OBSP \$100 per diagnostic assessment for OBSP-

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3 screened women only, which mandates data collection through the ICMS. One of the data
4 elements in the ICMS identifies whether an OBSP-screened patient was diagnosed at an O-
5 BAS. In order to ascertain whether OBSP-screened patients underwent diagnostic assessment
6 at an the O-BAS status for the ICMS only collects data on OBSP-screened women. To
7 determine whether GP-screened and symptomatic patients were assessed at an O-BAS, we
8 used the location of the patients' biopsy from billing data, OHIP, supplemented with the location
9 of the patients' surgery (**Supplementary Table S1**).^{12,15} Using the OBSP-screened cohort for
10 validation, we achieved a sensitivity of 95% and a specificity of 80%.

11 12 13 14 15 16 17 18 19 20 21 **Healthcare utilization**

22
23 We explored the frequency and timing of various diagnostic tests and consultations or visits with
24 various healthcare providers 6 months before diagnosis until the date of first treatment. We
25 searched the OHIP database (physician billing) database in addition to the hospital-based
26 databases Discharge Abstract Database (DAD) and the National Ambulatory Care Reporting
27 System (NACRS). Administrative codes are reported in **Supplementary Tables S2-3**.

28 29 30 31 32 33 34 35 **Diagnostic interval**

36
37 We defined the diagnostic interval as the time from suspicion of breast cancer until the
38 diagnosis date from the OCR. For screen-detected cancers, this is the suspicion date of
39 corresponds to the screening mammogram and is derived identified either from the ICMS
40 (OBSP-screened) or OHIP records (GP-screened patients). For symptomatic patients, we
41 searched OHIP, DAD, and NACRS for any relevant diagnostic procedures, consults, and visits,
42 and primary care referrals occurring within pre-specified look-back periods using.¹⁶ The
43 methodology suspicion date corresponds to the earliest healthcare encounter related to the
44 breast cancer diagnosis, incorporating the time spent in primary care published elsewhere
45 (Supplementary Tables S4).^{16,17} ~~For screen-detected cancers, this is the date of the screening~~

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~~mammogram and is derived either from the ICMS (OBSP-screened) or OHIP (GP-screened patients). For symptomatic patients, we searched OHIP, DAD, and NACRS for any relevant diagnostic procedures, consults, and visits occurring within pre-specified look-back periods.¹⁸~~

Pre-treatment interval

We defined the pre-treatment interval as the time from diagnosis until treatment started using the earliest of breast resection. ~~We determined the date of first treatment using the earliest of breast cancer surgery (Supplementary Table S2), any anti-neoplastic systemic therapy, or chest radiation applied to the chest. Antineoplastic therapy was identified from Breast cancer surgery was defined using OHIP, DAD, or NACRS. Systemic therapy included chemotherapy, targeted therapy, or hormonal therapy captured in the Activity Level Reporting (ALR) database, the New Drug Funding Program database, or the Ontario Drug Benefits database.~~ Any antineoplastic therapy was also obtained from DAD, or and NACRS. Radiation was identified from ALR.

Other covariates

We used the Collaborative Staging database to identify overall cancer stage (AJCC 7th edition), and the tumors' estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2) 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. ~~Patients with no hospital encounters within this window were considered to have no comorbidity (Supplementary Figure S2).^{18,19} To obtain s~~ Sociodemographic characteristics were derived from the , we linked the patients' postal code at the time of diagnosis to the Census using the Postal Code Conversion FilePCCF+ (version 7BA for income and rurality; (version 6C was used for immigrant density). Health insurance numbers were used for linkage across databases. All databases employed are used for continuous system performance monitoring and undergo routine quality checks.

Statistical methods

We present ~~the means~~ (standard deviation, SD), medians (interquartile range, IQR), and proportions, where appropriate. We used bivariate or multinomial logistic regression ~~or multinomial logistic regression~~ to compare factors between groups, reporting odds ratios (OR) and 95% confidence intervals (CI). We used linear regression to explore factors associated with wait-times, reporting beta coefficients and 95% CI, which represent the change in wait times (in days) per unit change in the covariate. Absence of heteroscedasticity was confirmed using the autoreg procedure. We used Cox proportional hazards regression to explore factors associated with all-cause mortality, reporting hazard ratios (HR) and 95% CI. Follow-up started at the time of diagnosis and ended at death or the last known healthcare encounter occurring on or before December 31, 2019. For OBSP-screen-detected cancer patients, lead-time bias was corrected by subtracting $[1 - \exp(-\lambda t)] / \lambda$ from the survival time, where λ is the inverse of the mean sojourn time (2 years) and t is the survival time.²⁰ -The date of death was assigned using the OCR, supplemented with the Registered Persons Database. Unless otherwise stated, all multivariable models were adjusted for O-BAS status, screened/symptomatic presentation, age, sex, neighbourhood income quintile, neighbourhood immigrant density, rurality, Charlson comorbidity index, prior breast/non-breast cancer history, cancer laterality, cancer stage, hormone receptor profile, topography, and geography (Local Health Integration Network, LHIN). Proportionality was confirmed by visual inspection of Kaplan-Meier plots, log(-log) survival plots, and Loess-smoothed Schoenfeld residuals versus time. All analyses were performed using SAS version 9.4 (Cary, NC, SAS Institute Inc.). Statistical tests were two-sided and evaluated at a 5% significance level. All cells <6 were suppressed. Ethics approval was not required.

Results

Optimizing care for symptomatic breast cancer patients

A total 51,460 breast cancer patients were identified (**Supplementary Figure S3**). The mean age at diagnosis was ~~Patients were a mean~~ 63 (SD 13.7) years ~~of age at diagnosis~~, 86% had no comorbidity, 3,845 (7%) had a prior breast cancer and 42,598 (83%) were diagnosed in an O-BAS (**Table 1**). A total 28,107 (55%) were symptomatic, 13,615 (27%) were OBSP-screened, and 9,738 (19%) were GP-screened. ~~Most patients had stage 1 (n=21,218; 42%) or stage 2 (n=18,568; 37%) breast cancer.~~

O-BAS vs. non-O-BAS

After adjustment, O-BAS patients were more likely to be younger ~~[OR 0.86 (0.84-0.88) per 10 years]~~, have no comorbidities ($p=0.0008$), live closer to an O-BAS ~~[OR 0.34 (0.29-0.41) per 100km]~~, and live in a higher-income urban neighbourhood ~~with the least immigrant density~~ ($p<0.0001$ ~~for all for all~~) (**Table 1**). ~~The likelihood of being diagnosed in an O-BAS did not change over the study period (p=0.81). While there was no difference by disease laterality (p=0.32) or hormone receptor status (p=0.59), O-BAS patients were more likely to have had lower-stage breast cancers disease (p<0.0001), known hormone receptor status (p<0.0001), were more likely to have had a greater risk of a prior breast cancer (p=<0.00054), and were more likely to have had an screen-detected [been OBSP-screened cancer [OR 1.684 (1.4957-1.7480)] or ; or GP-screen-detected cancer [ed OR 1.49-31 (1.4023-1.2941)] than symptomatic than symptomatic cancer.~~

OBSP-screened, GP-screened, versus symptomatic

The proportion of ~~breast cancer~~ patients who were OBSP-screened increased from 23% in 2013 to 29% in 2017 with ~~a correspondingly decline in breast cancer fewer~~ patients presenting with symptoms (**Figure 1A**). ~~In a sensitivity analysis restricted to women aged 50-74 years with no prior breast cancer history (the OBSP-eligible cohort), we observed a similar increase over time,~~

~~but the proportion of women with breast cancer who were OBSP-screened surpassed the symptomatic group after 2014, reaching 44% by 2017 (Figure 1B).~~

Symptomatic patients were more likely to reside in a lower-income neighbourhood ($p < 0.0001$), have greater comorbidity (~~76% versus 81% had no comorbidity~~ $p < 0.0001$), and have advanced-stage breast cancer than screened patients: 30% of symptomatic patients had stage 1 cancer compared with 47% of GP-screened and 64% of OBSP-screened patients (Table 2). ~~Although the majority of patients diagnosed with breast cancer were female, males were more likely to be symptomatic ($p < 0.0001$).~~ Symptomatic patients were more likely to have biologically more aggressive disease: 18% had ER- tumors (versus 11% for OBSP-screened) and 18% had HER2+ tumors (versus 12% for OBSP-screened).

The diagnostic interval

~~The date of suspicion was identifiable for 47,840 (93%) patients (Supplementary Table S4).~~

The diagnostic interval was a median 35 (IQR 19, 82) days. Diagnosis at an O-BAS did not reduce the diagnostic interval [beta ~~-2.0 (-3.7, -0.4)~~ ~~-1.6 (-3.4, 0.3)~~ days] (Table 3) ~~or~~. ~~We divided the diagnostic interval into~~ shorter sub-intervals (e.g. time from suspicion to first image test), ~~but little variability was observed between O-BAS and non-O-BAS patients (Supplementary Table S5).~~ In contrast, ~~stage was a significant predictor:~~ compared with stage 1, the diagnostic interval was 10, 12, 21, and 6-10 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 [beta ~~-10.3 (-17.0, -3.6)~~ ~~-9.9 (-17.7, -2.1)~~ days], as did males [beta ~~-13.0 (-19.7, -6.3)~~ ~~-11.1 (-18.7, -3.5)~~]. Compared with symptomatic patients, the diagnostic interval was 25 days shorter [beta ~~-24.8 (-26.3, -23.4)~~ ~~-25 (-27, -23)~~] for OBSP-screened patients and 6-5 days longer [beta 4.9 (3.3, 6.4) 6 (4, 7) days] for GP-screened patients. No other demographic and clinical factors were meaningfully associated with the length of the diagnostic interval.

The pre-treatment interval

The first intervention provided was surgery for 40,652 (79%) and systemic therapy for 9,296 (18%) of patients. The pre-treatment interval was a median 34 (IQR 23, 47) days. After adjustment, there were no factors associated with a meaningful delay ~~>7 days~~ (Table 3).

Healthcare utilization

Frequency: O-BAS patients were more likely to have received various diagnostic tests before treatment than non-O-BAS patients, including a diagnostic mammogram (91% versus 78%), screening mammogram (44% versus 30%), breast biopsy (97% versus 85%), breast ultrasound (94% versus 82%), and breast MRI (23% versus 13%) (Table 4). However, O-BAS patients were less likely than non-O-BAS patients to have had an abdominal/thoracic CT scan (25% versus 38%) and a chest x-ray (39% versus 49%). O-BAS patients were more likely than non-OBAS patients to have a consultation with a general surgeon or general thoracic surgeon (97% versus 87%), ~~but, Conversely, O-BAS patients~~ were less likely than non-O-BAS patients to visit their GP (40% versus 49%), ~~or~~ have a consultation with an internist (18% versus 24%), or medical oncologist (15% versus 26%).

Timing: ~~Before first treatment,~~ O-BAS patients had a consultation or visit with a general surgeon or general thoracic surgeon earlier than non-O-BAS patients (median 8 days versus 1 day before diagnosis) (Table 4). The time from diagnosis until consultation with a medical oncologist or radiation oncologist was longer, with a median 20 (11, 32) days and 21 (10, 34) days, respectively. ~~Seven percent of patients consulted with a dermatologist a median 84 (27, 140) days after diagnosis.~~

Overall survival

Patients were followed a mean 42 (SD 21.5) months after diagnosis. After adjustment, patients diagnosed at an O-BAS had better overall survival than non-O-BAS patients [~~crude~~ HR 0.73 (0.69-0.78) 0.39 (0.37, 0.41)] (Table 5). After adjustment, overall survival was also better for patients diagnosed in an O-BAS [HR 0.74 (0.69-0.80)] and for patients who were either OBSP-screened [HR 0.73 (0.66-0.80) 0.47 (0.42-0.52)] or GP-screened [HR 0.67 (0.62-0.72) 0.69 (0.63-0.76)] versus symptomatic. Without adjustment, O-BAS had a larger impact on survival among symptomatic patients [HR 0.43 (0.41-0.45), $p < 0.0001$], and GP-screened patients [HR 0.48 (0.41-0.56), $p < 0.0001$] than OBSP-screened patients [HR 0.69 (0.55-0.88), $p = 0.002$] (p -interaction = 0.0003) (Figure 2). In the adjusted model, the difference of the effect of O-BAS on overall survival was similar across patient types (p -interaction=0.9180): HR 0.73 (0.6769-0.7978), $p < 0.0001$ for among symptomatic, HR 0.763 (0.62-0.9864), $p = 0.00024$ among for GP-screened, and HR 0.752 (0.56-0.992), $p = 0.0085$ among for OBSP-screened. Patients also had worse overall survival if they were older [HR 1.51 (1.48-1.55) per 10 years], lived in a lower-income neighborhood [HR 1.36 (1.23-1.50) for the lowest versus the highest], had greater comorbidity [HR 2.57 (2.28-2.90) for 3+ versus 0 comorbidity] or prior cancer history, had more advanced stage ($p < 0.0001$), or had triple-negative disease ($p < 0.0001$ for all) (Table 5).

We also explored whether wait times were associated with overall survival. After adjustment, a longer diagnostic interval was not associated with worse overall survival ($p = 0.09$), nor was there evidence of a trend (Table 5). In contrast, a longer pre-treatment interval was associated with better overall survival ($p < 0.0001$) with a gradient response until 8 weeks after diagnosis.

Discussion

In this study, we found that ~~patients screened in an organized program~~ ~~OBSP-screened patients~~ had a faster time until diagnosis and were more likely to be referred to an O-BAS ~~than symptomatic patients~~. We also observed that attendance at an O-BAS was associated with improved overall survival ~~independently of wait-times, route to diagnosis, or stage~~.

As of 1998, the OBSP implemented a process where screened women 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 work-up.⁹ The main focus of this system-level change was to improve the coordination and quality of care for women screened through the OBSP. Our results demonstrate the success of this program, but similar improvements are needed for symptomatic patients for several reasons (**Figure 3**).²¹ First, symptomatic patients exhibit features associated with worse prognosis, including older age at diagnosis, more advanced stage, and more biologically aggressive (~~e.g. undifferentiated~~) tumors.^{22–26} O-BAS are high-volume centres that are equipped to manage complex patients and efficiently ~~render a diagnosis~~ ~~se patients with breast cancer~~.^{9,27} Despite this, symptomatic patients were less likely to be diagnosed at an O-BAS (**Figure 3, a-c**). Second, a shorter time until treatment (diagnostic plus pre-treatment intervals) may be important for a subset of patient with more aggressive tumors.²⁸ Patients with fast-growing tumors are less likely to be screen-detected due to length time bias, so any effect of wait times on mortality is expected to be more ~~poignant~~ ~~impactful~~ ~~among the for~~ symptomatic patients, ~~yet~~.^{26,27} ~~Despite this,~~ symptomatic patients had a longer time until diagnosis (**Figure 3, d-e**).^{29,30} Third, anxiety during the diagnostic interval is high, and may be higher for patients with symptoms ~~than those without~~.^{14,31,32} Thus, symptomatic patients ~~are expected to~~ ~~may again~~ derive ~~the greater~~ ~~rst~~ benefit from a shorter diagnostic interval. In addition, ~~patients are more likely to feel some comfort if there is less uncertainty around their symptoms~~. ~~With~~ comprehensive data collection for the OBSP-screened population, patients

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3 can learn about their risk of having cancer given an abnormal screen. There is no parallel for ~~the~~
4 symptomatic patients who, arguably, may need this type of information more urgently than
5 asymptomatic women do (**Figure 3, e-g**).^{33,34}
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10 The OBSP requires that O-BAS adhere to ~~the~~ requirements outlined in its standard
11 operating procedures, ~~including quality standards and wait-time targets~~.^{17,35} Additionally, O-BAS
12 are required to develop mechanisms for ongoing evaluation and quality improvement, and to
13 implement processes to notify the referring physician of abnormal test results, recommendations
14 for biopsy, and the diagnosis ~~reached~~. However, approximately 74% of all breast cancer cases
15 are diagnosed outside the auspices of the ~~OBSP-organized screening program (GP-screened or~~
16 ~~symptomatic), and as such, and~~ are therefore not subject to those same standards, reporting,
17 and performance management requirements. Funneling symptomatic patients through an the
18 OBSP-organized system is therefore expected to improve clinical and patient-reported
19 outcomes, and provide data necessary to inform quality improvement. ~~At the population level,~~
20 ~~this is expected to have a large impact on system performance.~~
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34 ~~Our findings support extending the OBSP-organized screening program referral~~
35 ~~pathways and resources to include symptomatic patients. Although this subpopulation~~
36 ~~comprises 74% of all breast cancer diagnoses, We suspect~~ the existing O-BAS likely have the
37 capacity to evaluate these patients because by 2017, 79% of all symptomatic breast cancer
38 patients in the province were diagnosed at an O-BAS (this estimate has increased since the
39 time of writing as more centres have become O-BAS). While it remains unknown how many
40 symptomatic patients without breast cancer are assessed at an O-BAS, we suspect that O-BAS
41 are also ruling-out cancer in many of these patients because: 1) the likelihood of a cancer
42 diagnosis is higher if symptoms are present; 2) the need for a diagnostic biopsy is more likely
43 for symptomatic patients; and 3) O-BAS are more likely to have the ability to perform a biopsy
44 than non-O-BAS.^{11,36} It remains possible that increased referrals to O-BAS will result in capacity
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constraints and prolonged wait-times. This should be considered when designing system-level changes to the diagnostic process for symptomatic women. However, a more standardized diagnostic assessment pathway may also reduce repeated imaging and unnecessary testing, which is also expected to reduce costs.³⁷ A 2018 environmental scan of national and regional cancer diagnostic improvement initiatives described ~~reported costs and cost savings, but formal cost effectiveness analyses were not available.~~⁵ Such analyses should be considered prior to full implementation of O-BAS.

Our results support that symptomatic patients should receive more streamlined care aligned with the OBSP screening practices, despite some limitations. ~~One limitation of this study is the risk of misclassification~~ First, there may be some misclassification of GP-screened ~~cancers patients~~ (e.g. some may have been symptomatic) and symptomatic ~~cancers patients~~ (e.g. some may have been ~~incidental but incidental findings~~ ~~ssly diagnosed~~). However, the demographic, clinical, and tumor characteristics of the GP-screened group was in-between that of the OBSP-screened and symptomatic groups, suggesting that this misclassification is small. Further, the rate of incidental breast cancer detection is believed to be low ~~and is unlikely to alter our conclusions.~~³⁸⁻⁴⁰ Second, the gold standard definition of O-BAS (~~from the ICMS~~) is imperfect: it reflects the institution that renders the diagnosis, which may differ from the institution conducting the remainder of the diagnostic work-up. Also, there are some institutions that ~~behave function~~ like an O-BAS (e.g. have all the necessary equipment and personnel), but they do not have patient navigation or a funding agreement with the OBSP. ~~Therefore these~~ ~~These~~ centres were classified as non-O-BAS, despite ~~potentially functioning like~~ ~~having some~~ an O-BAS ~~features~~. ~~Third, although males diagnosed with breast cancer had significantly worse overall survival than females, results may not generalize to this group.~~ ~~Fourth~~ ~~Third~~, patients with prior breast cancers had a significantly longer diagnostic interval than those who did not. However, because the suspicion algorithm was developed in a cohort of first-ever

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breast cancer patients, it may not be generalizable to valid in this subgroup of patients.^{16,17}

Nevertheless, findings from a recent systematic review recommend that patients with a prior history of breast cancer be included in screening programs (even if not high-risk), a conclusion that is supported by our findings.⁴¹ Fourth, information on sociodemographic factors were limited to neighbourhood-level classification rather than individual-level, which may result in misclassification on estimates of income and immigrant density. Fifth, our results may not generalize to certain patient groups, like males. scenarios. For example, results may not generalize to males because breast cancer may be considered an entirely different entity compared with females. Further, our results may not generalize to patients who are diagnosed with ductal carcinoma *in situ*, which was out-of-scope in the present analysis because it is generally asymptomatic. The small number of patients classified as stage 0 are likely misclassified. Lastly/Finally, our results may not generalize to other jurisdictions that do not have organized screening programs or have a designated referral stream for symptomatic women. While other provinces in Canada have organized screening programs, we are unaware of any provincial-level assessment programs designated for symptomatic women.^{37,42,43} Reviews of the literature related to symptomatic presentation often focus only on wait-times as a measure of performance.^{44,45}

In conclusion, the efficiency and effectiveness of the OBSP referral patterns has created a high-quality mechanism for screen-eligible patients to receive a timely breast cancer diagnosis and optimal care. Our findings suggest that all individuals with signs and symptoms of breast cancer would benefit from the organized, high-quality diagnostic assessment processes and standards like those employed by the OBSP. There exists-is a clear need to leverage the existing infrastructure of the OBSP and extend provincial oversight and performance monitoring for all individuals undergoing breast cancer assessment for a possible cancer diagnosis. relevant of the current pandemic organized screening in Ontario⁴⁶

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Data availability statement: Ontario Health is prohibited from making the data used in this research publicly accessible if it includes potentially identifiable personal health information and/or personal information as defined in Ontario law, specifically the Personal Health Information Protection Act (PHIPA) and the Freedom of Information and Protection of Privacy Act (FIPPA). Upon request, data de-identified to a level suitable for public release may be provided.

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Supplementary figures

Figure S1: Classification of patients as OBSP-screen-detected, GP-screened, or symptomatic. Patients were classified as OBSP-screened if their cancer diagnosis in the Ontario Cancer Registry was associated with a cancer diagnosis detected from the OBSP database. All remaining patients (non-OBSP-screened) were considered to have been screened by their general provider (GP-screened) if they had a screening mammogram within 1 year of diagnosis. All remaining patients were classified as symptomatic.

OBPS – Ontario Breast Screening Program; O-BAS – OBSP-affiliated breast assessment site; ICMS - Integrated Client Management System (database that tracks OBSP-screened clients)

Supplementary Figure S2: Rationale for classifying missing comorbidity as no comorbidity using overall survival as an outcome indicator.

Supplementary Figure S3: Patient selection. OHIP – Ontario Health Insurance Plan database.

Supplementary tables

Supplementary Table S1: List of institutions and associated institution numbers of O-BAS at the time of analysis. The assessment centre start date is the date the institution became affiliated with the OBSP (e.g. met the criteria to be considered an O-BAS and a funding agreement was enacted with the Ontario Ministry of Health). OBPS – Ontario Breast Screening Program; O-BAS – OBSP-affiliated breast assessment site

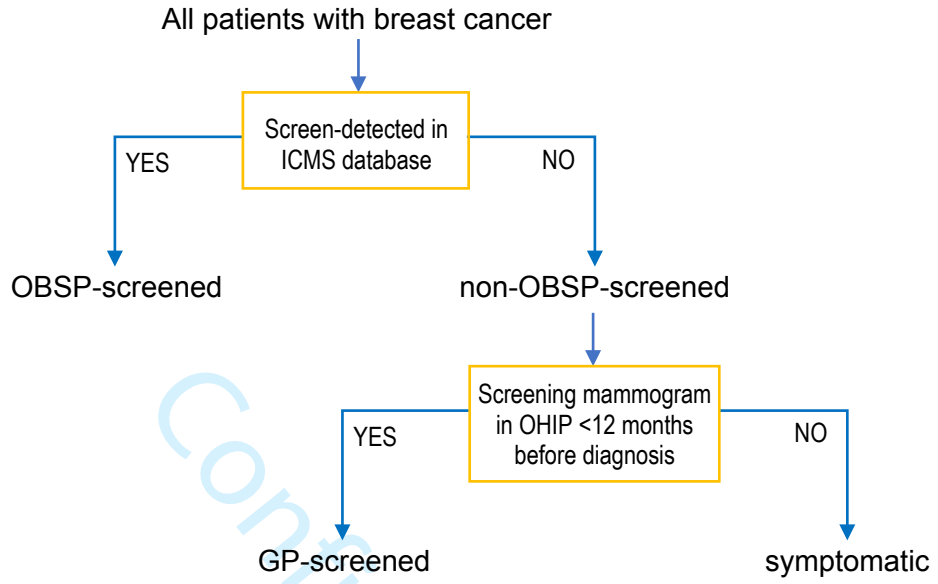
Supplementary Table S2: Administrative codes to identify the date of surgery.

Supplementary Table S3: Administrative codes to identify the date of various diagnostic tests, consultations and visits, and imaging.

Supplementary Table S4: Healthcare encounters observed the suspicion date. If multiple encounters (e.g. diagnostic tests or consults) were observed on this date, the one chosen was based on a hierarchy.

Supplementary Table S5: Length of various subintervals measured between the date of suspicion and the date treatment started.

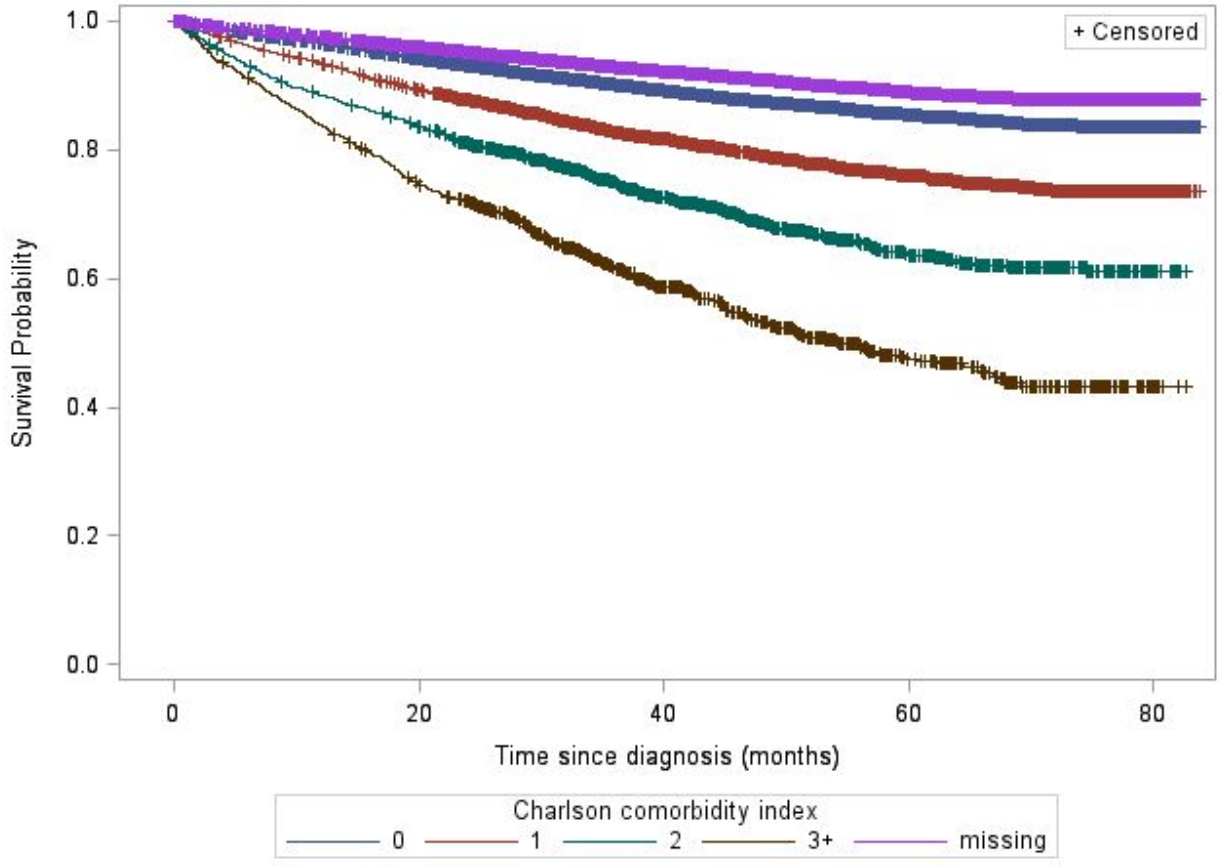
Supplementary Figure S1: Categorization of patients as OBSP-screen-detected, GP-screened, or symptomatic



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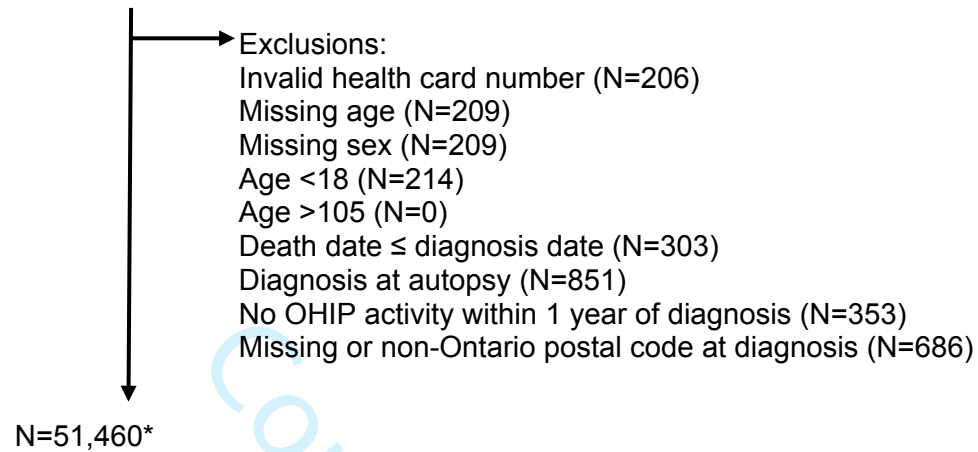
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Supplementary Figure S2: Kaplan-Meier plot for overall survival by Charlson comorbidity score



Supplementary Figure S3: Patient selection

Number of unique patients with a breast cancer diagnosis between 2013 and 2017 (ICD-O-3 topography code C50; ICD-O-D behavior code = 3) (N=52,642)*



*Cohort includes only unique patients.

1. For patients with bilateral breast cancer on the same day (i.e. same histology, same diagnosis date) and different laterality, we created a 'bilateral' flag for these patients and kept their record with the higher stage
2. If patient had multiple primaries during time period, we kept their earliest record.

Supplementary Table S1: List of Ontario Breast Screening Program (OBSP)-affiliated Breast Assessment Sites (O-BAS)

Ontario facilities designated as an O-BAS that provide organized assessment must have certified mammography technologists and equipment that meets or exceeds that specified by Canadian Association of Radiologist's Mammography Accreditation Program (CAR-MAP); provide all abnormal mammographic work-up, including special mammographic views and image-guided core biopsy; provide radiological, surgical and pathologic consultation with experts in breast evaluation; and provide navigation for patient support and coordination of referrals.

To determine whether GP-screened and symptomatic patients were assessed at an O-BAS, we used the location of the patients' biopsy from billing data, supplemented with the location of the patients' surgery.^{12,15} Using the OBSP-screened cohort for validation of this approach, we achieved a sensitivity of 95% and a specificity of 80% for the O-BAS designation.

Clinic Name	Assessment Centre Start Date	Institution Numbers
Ottawa Hospital - Civic Campus	October 29, 1998	4046; 4079
Listowel Memorial Hospital	November 1, 1999	1740
Timmins and District Hospital	January 1, 2000	3414; 4123
Health Sciences North	October 15, 2000	4059; 4063
Renfrew Victoria Hospital	March 1, 2001	1813; 4184
Hotel Dieu Hospital	July 1, 2001	4106; 4105
St. Joseph's Hospital (London)	March 1, 2002	1497; 4255
Pembroke Regional Hospital	March 15, 2002	1804; 4071
Greater Niagara General Hospital	April 1, 2002	3982; 4213
St. Catharine's General Hospital	April 1, 2002	4045; 4224
Welland County General Hospital	April 1, 2002	3978; 4227
St. Michael's Hospital	August 1, 2002	1444; 3985
Dixie X-Ray Associates - Finch	March 10, 2003	N/A
Winchester District Memorial Hospital	April 4, 2003	4267
Grey Bruce Health Services - Owen Sound	October 20, 2003	3944; 4131
St. Joseph's Healthcare Hamilton - King Campus	November 20, 2003	N/A
Windsor Regional Hospital - Metropolitan Campus	January 26, 2004	1079; 4414
Stratford General Hospital	October 5, 2004	1754; 4168

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Chatham Centre	October 14, 2005	1223; 4238
Thunder Bay Regional Health Sciences Centre	March 27, 2006	3853; 4315
Vaughan Imaging Consultants	April 1, 2006	N/A
Princess Margaret Hospital	May 1, 2006	4406; 3910
Lakeridge Health - Oshawa	September 25, 2006	4171
Lakeridge Health - Bowmanville	September 25, 2006	N/A
Grand River Hospital - Freeport	July 30, 2007	3734; 4107
Wentworth-Halton X-Ray and Ultrasound - Burlington South	February 1, 2008	1160; 4144
Woodstock General Hospital	May 1, 2008	1716; 4057
Hawkesbury and District General Hospital	July 1, 2008	1777; 4268
Credit Valley Hospital	January 19, 2009	4747; 4751
Sault Area Hospital	April 1, 2009	3972; 4407
Juravinski Hospital & Cancer Care Centre**	August 10, 2010	N/A
Trenton Memorial Hospital	September 7, 2010	4099
WRH Breast Health - Ouellette Campus (formerly Hotel Dieu)**	January 4, 2011	4773; 4774; 4142
Markham Stouffville Hospital	January 17, 2011	3587; 4235
Uxbridge Cottage Hospital	January 17, 2011	N/A
Bluewater Health - Norman	June 1, 2011	4109; 4415
Peterborough Regional Health Centre	June 24, 2011	1768; 4073
Sensenbrenner Hospital	July 1, 2011	N/A
Kirkland and District Hospital	July 1, 2011	
Hôpital Notre-Dame Hospital	July 1, 2011	N/A
Weeneebayko General Hospital	July 1, 2011	
Women's College Hospital	July 4, 2011	4631
Sunnybrook Health Sciences Centre	July 4, 2011	3936; 4205
Scarborough Health Network - General	August 15, 2011	3975; 4152
Scarborough Health Network - Centenary	November 1, 2011	3943; 4139
Southlake Regional Health Centre	November 1, 2011	2038; 4001
Ross Memorial Hospital	November 1, 2011	1893; 4177
Etobicoke General Hospital	November 7, 2011	3929; 4245
Brampton Civic Hospital	November 7, 2011	4016; 4681; 4685
Mount Sinai Hospital	November 14, 2011	1423; 4110; 4804; 4805
Merivale Medical Imaging	April 1, 2012	N/A
Hôpital Montfort	April 1, 2012	1661; 4130; 4461
North York General - Branson	April 1, 2012	4234
Royal Victoria Regional Health Centre	October 29, 2012	1825; 3987
Brantford General Hospital	November 14, 2012	4675; 4679
St. Joseph's Healthcare Hamilton - Charlton Campus	November 15, 2012	2003; 4054; 4055
OBSP Hamilton*	April 1, 2013	4014; 4140
Lakeridge Health - Ajax Pickering Hospital*	June 1, 2013	4104
North Bay Regional Health Centre*	April 1, 2014	4730; 4734
South Bruce Grey Health Centre - Walkerton*	May 1, 2014	1330; 4233
York Radiology Consultants***	May 1, 2014	1983; 4285

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Georgetown Hospital*	July 1, 2014	3926; 4192
Northumberland Hills Hospital*	July 7, 2014	1681; 3970
Juravinski Hospital	October 1, 2014	4039
Mackenzie Health*	December 1, 2014	1515
Oakville-Trafalgar Memorial Hospital*	February 1, 2015	4759
Queensway Carleton Hospital*	April 1, 2015	2046
North York General - General*	April 15, 2015	N/A
Dixie X-Ray Associates - Highpoint*	April 15, 2015	N/A
Queensway Health Centre*	April 18, 2015	4624
Strathroy Middlesex General Hospital*	January 4, 2016	3860; 4237
Erie Shores HealthCare - Leamington*	August 2, 2016	4231; 4298

The following institutions were identified as an O-BAS from algorithm, but corresponding assessment center is Unknown:
3984, 4048, 4085, 4180

* Site became a paid assessment center during study period

** Site closed during study period

*** Site became a paid assessment center during study period and was subsequently closed

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Supplementary Table S2: Administrative codes for surgery

Code	Description
Surgery (OHIP definition)	
R111	Integumentary system surgical procedures – operations of the breast – partial mastectomy or wedge resection for treatment of breast disease, with or without biopsy, e.g. carcinoma or extensive fibrocystic disease
R108	Integumentary system surgical procedures – operations of the breast – mastectomy – female (with or without biopsy), simple
R109	Mastectomy, radical or modified radical (with or without biopsy)
R107	Integumentary system surgical procedures – operations of the breast, excision, tumor or tissue for diagnostic biopsy and/or treatment, e.g. carcinoma, fibroadenoma or fibrocystic disease (single or multiple – same breast)
R117	Integumentary system surgical procedures – operations of the breast – mastectomy, radical or modified radical (with or without biopsy)
R148	Integumentary system surgical procedures – operations of the breast – mastectomy – male – unilateral for treatment of pathological male breast disease (with or without biopsy), e.g. carcinoma – simple
R149	Integumentary system surgical procedures – operations of the breast – mastectomy – male – unilateral for treatment of pathological male breast disease (with or without biopsy), e.g. carcinoma – subcutaneous with nipple preservation
Surgery (CIHI definition)	
1YM87	Excision partial, breast
1YM89	Excision total, breast
1YM91	Excision(modified) radical, breast
1YM90	Excision total with reconstruction, breast
1YM88	Excision partial with reconstruction, breast
1YM92	Excision radical with reconstruction, breast
1YK87	Excision partial, nipple
1YK90	Excision total with reconstruction, nipple
1YK89	Excision total, nipple
1YL89	Excision total, lactiferous duct
1YL87	Excision partial, lactiferous duct
Surgery (QBP definition, using CIHI)	
1YM87	Excision partial, breast
1YM91LAXXQ	Excision radical, breast using combined sources of tissue [e.g. local flap and tissue expander] modified or NOS
1YM87DA	Excision partial, breast using endoscopic approach with simple apposition
1YM87GB	Excision partial, breast using endoscopic guide wire (or needle hook) excision technique with simple apposition of tissue
1YM87LA	Excision partial, breast using open approach with simple apposition of tissue (e.g. suturing)
1YM87LAXXA	Excision partial, breast using open approach and full thickness autograft to close defect
1YM87LAXXE	Excision partial, breast using open approach and local flap (to close defect)
1YM87UT	Excision partial, breast using open guide wire (or needle hook) excision technique and simple apposition of tissue
1YM89LA	Excision total, breast without tissue repair
1YM89LAXXA	Excision total, breast with full thickness autograft
1YM89LAXXE	Excision total, breast using open approach and local flap
1YM91LA	Excision (modified) radical, breast without tissue
1YM91LAPM	Excision radical, breast with implantation of breast prosthesis modified or NOS

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4	1YM91LATP	Excision (modified) radical, breast with implantation of tissue expander
5	1YM91LAXXA	Excision radical (modified), breast using full thickness autograft
6	1YM91LAXXE	Excision (modified) radical, breast using local flap
7	1YM91TR	Excision extended radical, breast without tissue
8	1YM91TRXXA	Excision extended radical, breast using full thickness autograft
9	1YM91TRXXE	Excision extended radical, breast using local flap
10	1YM91WP	Excision super radical, breast without tissue
11	1YM91WPXXA	Excision radical, breast using autograft super [Wangensteen
12	1YM91WPXXE	Excision super radical, breast using local flap
13	1YM88LAPM	Excision partial with reconstruction, breast without tissue with implantation of prosthesis
14	1YM88LAPME	Excision partial with reconstruction, breast with local flap with implantation of prosthesis
15	1YM88LAPMF	Excision partial with reconstruction, breast using free flap with implantation of prosthesis
16	1YM88LAPMG	Excision partial with reconstruction, breast using distant pedicled flap with implantation of prosthesis
17	1YM88LAPMK	Excision partial with reconstruction, breast using homograft with implantation of prosthesis
18	1YM88LAQF	Excision partial with reconstruction, breast without tissue with implantation of prosthesis and expander
19	1YM88LAQFE	Excision partial with reconstruction, breast with local flap with implantation of prosthesis and expander
20	1YM88LAQFF	Excision partial with reconstruction, breast using free flap with implantation of prosthesis and expander
21	1YM88LAQFG	Excision partial with reconstruction, breast using distant pedicled flap with implantation of prosthesis and ex
22	1YM88LATP	Excision partial with reconstruction, breast without tissue with implantation of tissue expander
23	1YM88LATPE	Excision partial with reconstruction, breast with local flap with tissue expander
24	1YM88LATPF	Excision partial with reconstruction, breast using free flap with implantation of tissue expander
25	1YM88LATPG	Exc prt breast w tiss expand ped flap reconstr
26	1YM88LATPK	Excision partial with reconstruction, breast using homograft with implantation of tissue expander
27	1YM88LAXXE	Excision partial with reconstruction, breast using local flap with no implanted device
28	1YM88LAXXF	Excision partial with reconstruction, breast using free flap with no implanted device
29	1YM88LAXXG	Excision partial with reconstruction, breast using distant pedicled flap with no implanted device
30	1YM90LAPM	Excision total with reconstruction, breast simple mastectomy with no node dissection without tissue with implantation of breast prosth
31	1YM90LAPME	Excision total with reconstruction, breast simple mastectomy with no node dissection using local flap with implantation of breast pros
32	1YM90LAPMF	Excision total with reconstruction, breast simple mastectomy with no node dissection using free flap (2) with implantation of breast p
33	1YM90LAPMG	Excision total with reconstruction, breast simple mastectomy with no node dissection using distant pedicled flap(1) with implantation
34	1YM90LAPMK	Excision total with reconstruction, breast using homograft with implantation of breast prosthesis
35	1YM90LAQF	Excision total with reconstruction, breast simple mastectomy with no node dissection without tissue with implantation of prosthesis an
36	1YM90LAQFE	Excision total with reconstruction, breast simple mastectomy with no node dissection using local flap with implantation of prosthesis
37	1YM90LAQFF	Excision total with reconstruction, breast simple mastectomy with no node dissection using free flap (2) with implantation of prosthes
38	1YM90LAQFG	Excision total with reconstruction, breast simple mastectomy with no node dissection using distant pedicled flap(1) with implantation
39	1YM90LATP	Excision total with reconstruction, breast simple mastectomy with no node dissection without tissue with implantation of tissue expand
40	1YM90LATPE	Excision total with reconstruction, breast using local flap with implantation of tissue expander
41	1YM90LATPF	Excision total with reconstruction, breast simple mastectomy with no node dissection using free flap (2) with implantation of tissue e
42	1YM90LATPG	Excision total with reconstruction, breast simple mastectomy with no node dissection using distant pedicled flap(1) with implantation
43	1YM90LATPK	Excision total with reconstruction, breast using homograft with implantation of tissue expander
44	1YM90LAXXE	Excision total with reconstruction, breast simple mastectomy with no node dissection using local flap with no implanted device
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1	1YM90LAXXF	Excision total with reconstruction, breast simple mastectomy with no node dissection using free flap (2) with no implanted device
2	1YM90LAXXG	Excision total with reconstruction, breast simple mastectomy with no node dissection using distant pedicled flap(1) with no implanted
3	1YM90LAXXQ	Excision total with reconstruction, breast with no implanted device using combined sources of tissue (e.g. free
4	1YM92LAPME	Excision (modified) radical with reconstruction, breast using local flap with implantation of breast prosthesis
5	1YM92LAPMF	Excision (modified) radical with reconstruction, breast using free flap with implantation of breast prosthesis
6	1YM92LAPMG	Excision (modified) radical with reconstruction, breast using distant pedicled flap with implantation of breast prosthesis
7	1YM92LAQFE	Excision (modified) radical with reconstruction, breast using local flap with implantation of prosthesis and expander
8	1YM92LAQFG	Excision (modified) radical with reconstruction, breast using distant pedicled flap with implantation of prosthesis and expander
9	1YM92LATPE	Excision (modified) radical with reconstruction, breast using local flap with implantation of tissue expander
10	1YM92LATPF	Excision (modified) radical with reconstruction, breast using free flap with implantation of tissue expander
11	1YM92LATPG	Excision (modified) radical with reconstruction, breast using distant pedicled flap with implantation of tissue expander
12	1YM92LATPK	Excision radical with reconstruction, breast modified or NOS using homograft with implantation of tissue expander
13	1YM92LAXXE	Excision (modified) radical with reconstruction, breast using local flap with no implanted device
14	1YM92LAXXF	Excision (modified) radical with reconstruction, breast using free flap with no implanted device
15	1YM92LAXXG	Excision (modified) radical with reconstruction, breast using distant pedicled flap with no implanted device
16	1YM92LAXXQ	Excision radical with reconstruction, breast modified or NOS with no implanted device using combined sources of
17	1YM92TRPME	Excision radical with reconstruction, breast extended [Urban] using local flap with implantation of breast prosthesis
18	1YM92TRPMK	Excision radical with reconstruction, breast extended [Urban] using homograft with implantation of breast prosthesis
19	1YM92TRTPE	Excision radical with reconstruction, breast extended [Urban] using local flap with implantation of tissue expander
20	1YM92TRTPK	Excision radical with reconstruction, breast extended [Urban] using homograft with implantation of tissue expander
21	1YM92TRXXE	Excision extended radical with reconstruction, breast using local flap with no implanted device
22	1YM92TRXXF	Excision extended radical with reconstruction, breast using free flap with no implanted device
23	1YM92TRXXQ	Exc rad w reconstr breast OA w ext rad excisn combo tis
24	1YM92WPPMK	Excision radical with reconstruction, breast super [Wangensteen] using homograft with implantation of breast prosthesis
25	1YM92WPTPK	Excision radical with reconstruction, breast super [Wangensteen] using homograft with implantation of tissue expander
26	1YM92LAPMK	Excision radical with reconstruction, breast modified or NOS using homograft with implantation of breast prosthesis
27	1YM92TRPMF	Excision radical with reconstruction, breast extended [Urban] using free flap with implantation of breast prosthesis
28	1YM92TRPMG	Excision radical with reconstruction, breast extended [Urban] using distant pedicled flap with implantation of breast prosthesis
29	1YM92TRTPF	Excision radical with reconstruction, breast extended [Urban] using free flap with implantation of tissue expander
30	1YM92TRTPG	Excision radical with reconstruction, breast extended [Urban] using distant pedicled flap with implantation of tissue expander
31	1YM92TRXXG	Excision radical with reconstruction, breast extended [Urban] using distant pedicled flap with no implanted device
32	1YM92WPPME	Excision radical with reconstruction, breast super [Wangensteen] using local flap with implantation of breast prosthesis

1YM92WPPMF	Excision radical with reconstruction, breast super [Wangensteen] using free flap with implantation of breast prosthesis
1YM92WPPMG	Excision radical with reconstruction, breast super [Wangensteen] using distant pedicled flap with implantation of breast prosthesis
1YM92WPTPE	Excision radical with reconstruction, breast super [Wangensteen] using local flap with implantation of tissue expander
1YM92WPTPF	Excision radical with reconstruction, breast super [Wangensteen] using free flap with implantation of tissue expander
1YM92WPTPG	Excision radical with reconstruction, breast super [Wangensteen] using distant pedicled flap with implantation of tissue expander
1YM87UTXXA	Excision partial, breast using open guide wire (or needle hook) excision technique with autograft (to close defect)
1YM87UTXXE	Excision partial, breast using open guide wire (or needle hook) excision technique with local flap (to close defect)
1YM92WPXXF	Excision radical with reconstruction, breast super [Wangensteen] using free flap with no implanted device
1YM92WPXXG	Excision radical with reconstruction, breast super [Wangensteen] using distant pedicled flap with no implanted device
1YM92WPXXQ	Excision radical with reconstruction, breast super [Wagensteen] using combined sources of tissue (e.g. free and pedicled TRAM flap) with no implanted device
1YK87LA	Excision partial, nipple using open excisional approach
1YK87LAXXA	Excision partial, nipple using open excisional approach and full thickness autograft
1YK87LAXXB	Excision partial, nipple using open excisional approach and split thickness autograft
1YK87LAXXE	Excision partial, nipple using open excisional approach and local flap [e.g. rotation, advancement, transposition, Z-plasty] for closure
1YK89LA	Excision total, nipple using open approach
1YK89LAXXA	Excision total, nipple using open approach and full thickness autograft
1YK89LAXXE	Excision total, nipple using open approach and local flap [e.g. rotation, advancement, transposition, Z-plasty]
1YK90LAXXA	Excision total with reconstruction, nipple using open approach and full thickness autograft [e.g. contralateral nipple, labia, thigh, retroauricular tissue]
1YK90LAXXE	Excision total with reconstruction, nipple using open approach and local skin flap [e.g. propeller, star, quadripod skate]
1YK90LAXXQ	Excision total with reconstruction, nipple using open approach and combined local flap [e.g. nipple] and autograft [e.g. areola]
1YL87LA	Excision partial, lactiferous duct using open approach
1YL89LA	Excision total, lactiferous duct using open approach
<p>Restricted to the following ICD-10 diagnostic codes: C00-C97, D050, D051, D057, D059, D24, D486, D0500, D0501, D0509, D0510, D0511, D0519, D0570, D0571, D0579, D0590, D0591, D0599, D038, D039, D048, D049, D097, D099, D197, D199, D367, D369, D487, D489.</p> <p>OHIP – Ontario Health Insurance Plan database; CIHI – Canadian Institute of Health Information, which includes data from hospital-based procedures (inpatient and outpatient); QBP – quality-based procedures (a definition of surgery established at Cancer Care Ontario)</p>	

Supplementary Table S3: Administrative codes for healthcare

utilization

Code	Source	Description
Diagnostic mammogram		
X184	OHIP	Unilateral Mammogram - for individuals with signs or symptoms or follow-up of established disease
X185	OHIP	Bilateral Mammogram - for individuals with signs or symptoms or follow-up of established disease
X194	OHIP	Additional coned views with or without magnification (limit of two per breast) per film
Screening mammogram		
X172	OHIP	Unilateral Mammogram - for individuals with identified risk factors in accordance with clinical practice guidelines
X178	OHIP	Bilateral Mammogram - for individuals with identified risk factors in accordance with clinical practice guidelines
Breast biopsy		
J149	OHIP	Ultrasonic guidance of biopsy, aspiration, amniocentesis or drainage procedures (one physician only)
X121	OHIP	Stereotactic core breast biopsy
Z141	OHIP	Needle Biopsy - one or more
Z143	OHIP	Needle Biopsy - large core breast biopsy - (14 gauge or larger bore needle)
2YK71	CIHI	Biopsy, nipple using percutaneous approach (needle, punch) or open [incisional] approach
2YM71	CIHI	Biopsy, breast using percutaneous (needle) aspiration, device NEC or ore needle aspiration technique
2SZ71	CIHI	Biopsy, soft tissue of the chest and abdomen using percutaneous (needle) approach or open [incisional] approach
Lymph node biopsy		
R914	OHIP	Axillary or inguinal lymph nodes - limited resection, unilateral
Z405	OHIP	Biopsy, Anterior cervical lymph node(s), unilateral
Z406	OHIP	Biopsy, Scalene, posterior cervical lymph node(s), unilateral
Z407	OHIP	Percutaneous retroperitoneal, one group
Z408	OHIP	Bone marrow core biopsy (with biopsy needle)
Z409	OHIP	Percutaneous retroperitoneal, two group
Z411	OHIP	Biopsy, Axillary or inguinal lymph node(s), unilateral
Sentinel node biopsy		
Z427	OHIP	Sentinel node biopsy, per draining basin
2MD71	CIHI	Biopsy, lymph node(s), axillary using percutaneous (needle) approach or open approach
Consultations and visits		
Internal medicine consult	OHIP	A135, A130, A435, A136, A133, A134, A138, C135, C130, C435, C136, C133, C134, C131, W235, W130, W435, W236
Dermatology consult	OHIP	A025, A027, A026, A023, A024, A020, C025, C026, C023, C024, C020, W025, W026
Cardiology consult	OHIP	A605, A600, A675, A606, A603, A604, A601, A608, A605, A600, A675, A606, A603, A604, A601, A608, C605, C600, C675, C606, C603, C604, C601 HSP specialty code = 60
General practitioner visit	OHIP	A005, A911, A912, A945, A905, A006, A003, A004, A888, A091, A900, A933, A100, A937, A967
Cardiac surgery consult	OHIP	A095, A935, A096, A093, A094, C095, C935, C096, C093, C094, W095, W096 HSP specialty code = 09
Medical oncology consult	OHIP	A445, A845, A446, A443, A444, A441, A448, C445, C845, C446, C443, C444, C441, W445, W765, W845, W44

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3	Radiation oncology consult	OHIP	A345, A765, A745, A346, A343, A340, A341, A348, C345, C765, C745, C346, C343, C344, C341
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5	General or general thoracic surgery consult	OHIP	A645, A935, A646, A643, A644, C645, C935, C646, C643, C644, A035, A036, A033, A034, C035, C935, C036, C033, C034, W035, W036
6			HSP specialty code = 03 (general surgery) or 64 (general thoracic surgery)
7			
8	Diagnostic radiology assessment	OHIP	A335, A365, A330, A332, A331, A338, C335, C365, C330, C332
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Breast ultrasound

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12	J127	OHIP	Diagnostic Ultrasound - scan B-mode (per breast)
13	3YM30	OHIP	Ultrasound, breast

Abdominal/thoracic ultrasound

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16	J128	OHIP	Abdominal scan - limited study (e.g. gallbladder only, aorta only or follow-up study)
17	J135	OHIP	Abdominal scan - complete
18	3OT30	CIHI	Ultrasound, abdominal cavity
19	3GY30	CIHI	Ultrasound, thoracic cavity

Abdominal/thoracic computed tomography (CT) scan

20			
21			
22	X406	OHIP	Thorax -without IV contrast
23	X407	OHIP	Thorax -with IV contrast
24	X125	OHIP	Thorax -with and without IV contrast
25	X409	OHIP	Abdomen -without IV contrast
26	X410	OHIP	Abdomen -without IV contrast
27	X126	OHIP	Abdomen -without IV contrast
28	3OT20	CIHI	Computerized tomography [CT], abdominal cavity
29	3YM20	CIHI	Computerized tomography [CT], breast
30	3GY20	CIHI	Computerized tomography [CT], thoracic cavity

Abdominal/thoracic magnetic resonance imaging (MRI) scan

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33	X446	OHIP	Breast - unilateral or bilateral, multislice sequence
34	X447	OHIP	Breast - unilateral or bilateral, repeat (another plane, different pulse sequence - to a maximum of 3 repeats).
35	X441	OHIP	Thorax - multislice sequence
36	X445	OHIP	Thorax - repeat (another plane, different pulse sequence - to a maximum of 3 repeats).
37	X451	OHIP	Abdomen - multislice sequence
38	X455	OHIP	Abdomen - repeat (another plane, different pulse sequence - to a maximum of 3 repeats).
39	X499	OHIP	Three Dimensional MRI acquisition sequence, including post-processing (minimum of 60 slices; maximum 1 per patient per day)
40	3OT40	CIHI	Magnetic resonance imaging [MRI], abdominal cavity
41	3YM40	CIHI	Magnetic resonance imaging [MRI], breast
42	3GY40	CIHI	Magnetic resonance imaging [MRI], thoracic cavity

Chest x-ray

43			
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45	X090	OHIP	Chest - single view
46	X091	OHIP	Chest - two views
47	X092	OHIP	Chest - three or more views
48	3GY10	CIHI	Xray, thoracic cavity

Other (ductogram, capsulotomy, capsulectomy)

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51	X192	OHIP	Mammary ductography
52	J037	OHIP	Mammary ductography
53	3YL10	CIHI	Xray, lactiferous duct
54	Z182	OHIP	Breast capsulectomy
55	Z135	OHIP	Open capsulotomy with or without replacement of breast prosthesis
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3 1YM72 CIHI Release, breast

4 OHIP – Ontario Health Insurance Plan database; CIHI – Canadian Institute of Health Information, which includes data from hospital-
5 based procedures (inpatient and outpatient)
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Confidential

Supplementary Table S4: Healthcare encounters on the suspicion date

Index Contact Encounter Category	N=47,840	%
OBSP abnormal breast screening	11,821	25%
Screening mammography	3,004	6%
Breast cancer	3,154	7%
Other related cancers	371	1%
Benign neoplasm/CIS	2,445	5%
Breast cyst, cystic disease, abscess, hypertrophy, other	6,423	13%
Lymph system–related conditions	76	0%
Diagnostic mammography and related procedures, with referral	11,534	24%
Diagnostic mammography and related procedures, no referral	742	2%
Breast ultrasound, with referral	4,248	9%
Breast ultrasound, no referral	190	<1%
Other ultrasound, with referral	1,074	2%
Other ultrasound, no referral	42	<1%
Surgical consult with no procedure, with referral	1,518	3%
Surgical consult with no procedure, no referral	25	<1%
Cyst aspiration or drainage, with referral	62	<1%
Cyst aspiration or drainage, no referral	6	<1%
Breast biopsy with or without ultrasound guidance, with referral	576	1%
Breast biopsy with or without ultrasound guidance, no referral	24	<1%
Mastectomy, with referral	<6	<1%
Mastectomy, no referral	<6	<1%
Breast MRI, with referral	128	<1%
Breast MRI, no referral	<6	<1%
Other MRI, with referral	194	<1%
Other MRI, no referral	24	<1%
Nuclear medicine, with referral	154	<1%
Nuclear medicine, no referral	<6	<1%

Healthcare encounters on the suspicion date. If more than one encounter was present on this date, a previously established hierarchy was used as per Groome et al (2019):

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 informatics*. 2019;3:1-10.

doi:10.1200/CCI.18.00131

OBSP – Ontario Breast Screening Program; CIS – Carcinoma *in situ*; MRI – magnetic resonance imaging

Supplementary Table S5: Subintervals

Time interval	Description	Statistic	Non-O-BAS (n=8,862)	O-BAS (n=42,598)	Total (n=51,460)
Pre-treatment interval	Time from diagnosis to first treatment	N (%)	7,386 (83%)	39,614 (93%)	50,232 (98%)
		Median (IQR), days	34 (21, 49)	34 (23, 47)	34 (23, 47)
		90% percentile, days	72	63	63
Total interval	Time from index contact to initial treatment (diagnosis or first treatment)	N (%)	7,788 (88%)	40,052 (94%)	47,840 (93%)
		Median (IQR), days	39 (20, 92)	35 (18, 79)	35 (19, 82)
		90% percentile, days	174	162	165
Breast imaging interval	Time from referring physician visit to first breast imaging (diagnostic mammogram, breast ultrasound or breast magnetic resonance imaging)	N (%)	6,982 (79%)	38,991 (92%)	45,973 (89%)
		Median (IQR), days	7 (3, 14)	7 (3, 14)	7 (3, 14)
		90% percentile, days	31	29	29
Surgical consult interval	Time from referring physician visit to first surgical consult (biopsy, cyst aspiration, mastectomy)	N (%)	6,670 (75%)	37,453 (88%)	44,123 (86%)
		Median (IQR), days	6 (3, 12)	6 (3, 10)	6 (3, 10)
		90% percentile, days	21	18	19
Biopsy interval	Time from referring physician/biopsying physician to first biopsy between index contact and diagnosis date	N (%)	6,492 (73%)	37,948 (89%)	44,440 (86%)
		Median (IQR), days	2 (2, 5)	2 (2, 4)	2 (2, 4)
		90% percentile, days	7	6	6
First assessment interval	Time from index contact to first diagnostic test/consult	N (%)	7,250 (82%)	38,934 (91%)	46,184 (90%)
		Median (IQR), days	11 (4, 31)	13 (6, 29)	13 (5, 29)
		90% percentile, days	89	80	82
First Assessment to Diagnostic Interval	Time from first diagnostic test to diagnosis date	N (%)	7,250 (82%)	38,934 (91%)	46,184 (90%)
		Median (IQR), days	20 (10, 42)	17 (8, 36)	17 (8, 36)
		90% percentile, days	113	100	102
Diagnostic interval	Time from index contact to diagnosis date	N (%)	7,788 (88%)	40,052 (94%)	47,840 (93%)
		Median (IQR), days	39 (20, 92)	35 (18, 79)	35 (19, 82)
		90% percentile, days	174	162	165

O-BAS – OBSP-affiliated breast assessment site; OBSP – Ontario Breast Screening Program; IQR – (25th, 75th percentile)