# Unwarranted imaging for distant metastases in patients with newly diagnosed ductal carcinoma in situ and stage I and II breast cancer

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**Background:** In 2012, the American Society of Clinical Oncology (ASCO) released a Choosing Wisely Top Five list that included a recommendation against ordering advanced imaging tests to screen for metastases among asymptomatic patients with early breast cancer. Our provincial breast cancer staging guideline was subsequently updated. We report on the use of unwarranted bone scanning (BS), computed tomography (CT), nonbreast magnetic resonance imaging (MRI) and positron emission tomography (PET) among women diagnosed with stage 0–II breast cancer in Alberta in 2011–2015.

**Methods:** The cohort was retrospectively ascertained from the Alberta Cancer Registry. We used additional provincial data sources to obtain information about diagnostic imaging tests completed from biopsy to surgical date plus 4 months. The reason for each BS, CT, MRI and PET was abstracted. We calculated the frequency of advanced imaging tests completed for routine metastatic screening.

**Results:** Of 10 142 patients included, 2887 (28.5%) had at least 1 advanced imaging test completed for routine metastatic screening. Of these 2887 patients, 438 (15.2%) had a follow-up BS, CT, MRI or PET, and 28 patients (1.0%) had a nonbreast image-guided biopsy. Use of routine advanced imaging tests did not change clearly over time.

**Conclusion:** Our results demonstrate persistent use of advanced imaging tests for routine metastatic screening among patients with stage 0–II breast cancer despite the release of the ASCO Choosing Wisely recommendations and the update of our provincial breast cancer staging guideline. Investigation of strategies for guideline translation to improve upon value-based care of patients with early breast cancer is warranted.

**Contexte** : En 2012, l'American Society of Clinical Oncology (ASCO) a publié sa liste de 5 interventions à « Choisir avec soin », dans laquelle elle recommandait notamment de ne pas recourir aux techniques d'imagerie de pointe pour le dépistage des métastases chez les patientes atteintes d'un cancer du sein peu avancé et asymptomatique. Nos lignes directrices provinciales pour la stadification du cancer du sein ont été mises à jour en conséquence. Nous faisons aujourd'hui état de l'utilisation injustifiée de la scintigraphie osseuse (SO), de la tomodensitométrie (TDM), de l'imagerie par résonnance magnétique (IRM) non mammaire et de la tomographie par émission de positrons (TEP) chez les femmes ayant reçu un diagnostic de cancer du sein peu avancé (stade 0-II) en Alberta entre 2011 et 2015.

**Méthodes** : La cohorte a été réunie de manière rétrospective à partir du registre albertain du cancer. Nous avons utilisé d'autres sources de données provinciales pour obtenir des renseignements sur les épreuves d'imagerie diagnostique effectuées entre les dates de la biopsie et les dates de la chirurgie plus 4 mois. Le motif invoqué pour recourir à chaque SO, TDM, IRM et TEP a été recueilli. Nous avons calculé la fréquence des épreuves d'imagerie de pointe effectuées pour un dépistage de routine des métastases.

**Résultats** : Sur les 10142 patientes incluses, 2887 (28,5%) avaient subi au moins 1 épreuve d'imagerie de pointe pour le dépistage de routine des métastases. Parmi ces 2887 patientes, 438 (15,2%) ont subi une SO, une TDM, une IRM ou une TEP de suivi et 28 patientes (1,0%) ont subi une biopsie non mammaire guidée par l'imagerie. L'utilisation de routine des épreuves d'imagerie de pointe n'a pas nettement changé avec le temps.

**Conclusion** : Selon nos résultats, l'utilisation des épreuves d'imagerie de pointe pour le dépistage de routine des métastases persiste chez les patientes atteintes d'un cancer du sein de stade 0–II, malgré la publication des recommandations Choisir avec soin de l'ASCO et la mise à jour de nos lignes directrices provinciales concernant la stadification du cancer du sein. Il faudra se pencher sur des stratégies pour améliorer l'adoption de lignes directrices relatives aux soins véritablement utiles pour les patientes atteintes d'un cancer du sein peu avancé.

**B** reast cancer is the most commonly diagnosed cancer among adult women in Canada, and the absolute number of new cases identified each year is increasing as a result of our growing and aging population.<sup>1</sup> Fortunately, owing to the implementation of organized screening programs, most women will be diagnosed with early-stage disease (ductal carcinoma in situ [DCIS], stage I or stage II breast cancer)<sup>1,2</sup> and will be treated successfully with primary surgery plus adjuvant radiation and/or systemic therapies where applicable. In Alberta, the 5-year relative survival for ductal carcinoma in situ and stage I breast cancer is 100%, and for stage II breast cancer it is 95%.<sup>3</sup>

As breast cancer is an important public health concern, opportunities to promote value-based care should be prioritized.<sup>4,5</sup> Clinical practice guidelines recommend against routine screening for metastases with diagnostic imaging tests among patients with early breast cancer who do not have suggestive symptoms, signs or biochemical abnormalities.6-10 The likelihood of having radiologically evident distant disease is low,<sup>11-13</sup> and hence use of routine staging tests would rarely change the therapeutic plan or alter outcomes. Furthermore, routine screening for metastases can increase patient anxiety, lead to further unnecessary tests and biopsies, delay definitive treatment and escalate health care costs.14-16 Despite published guidelines, imaging for metastases in early breast cancer has been common.<sup>17-22</sup> The issue of unnecessary imaging for metastases in early breast cancer was highlighted by the American Society of Clinical Oncology (ASCO) in their inaugural Top Five list, which was released on Apr. 4, 2012, in response to the American Board of Internal Medicine's Choosing Wisely campaign.<sup>23</sup> Subsequently, the Alberta Health Services clinical practice guideline on breast cancer staging was updated.8 The recommendation for routine bone scanning in the setting of stage II disease was removed and the Alberta Provincial Tumour Team on behalf of Alberta Health Services endorsed the prior recommendation that routine abdominal imaging for DCIS and stage I and II breast cancer was not required. We therefore hypothesized that the utilization of routine staging tests in the setting of early breast cancer would decrease over time. The aim of this study was to report on the use of advanced imaging tests among women diagnosed with DCIS and stage I and stage II breast cancer between Jan. 1, 2011, and Dec. 31, 2015, in Alberta. Although the ASCO Choosing Wisely recommendation specifically addressed bone scanning (BS), computed tomography (CT) and positron emission tomography (PET), we also included nonbreast magnetic resonance imaging (MRI) for the sake of completeness.

# METHODS

This retrospective, population-based cohort study was approved by the Health Research Ethics Board of Alberta Cancer Committee.

# Study population

The Surveillance and Reporting department of Cancer-Control Alberta is able to collect and link data from the Alberta Cancer Registry, the CancerControl electronic medical record (EMR), the Canadian Institute for Health Information (CIHI) National Ambulatory Care Reporting System and Discharge Abstract Database, and physician billings to Alberta Health. We queried the Surveillance and Reporting department of CancerControl Alberta to identify all patients with DCIS and stage I and stage II breast cancer diagnosed between Jan. 1, 2011, and Dec. 31, 2015. Pathologic stage was recorded by the Alberta Cancer Registry on the basis of the American Joint Committee on Cancer staging manual, seventh edition.<sup>24</sup> Any patients who did not undergo definitive breast cancer surgery (mastectomy or breast conservation plus sentinel node biopsy and/or axillary node dissection) were excluded. Furthermore, we excluded patients with stage III disease (where routine screening for metastases is warranted) and patients with de novo stage IV disease (whose metastatic classification may or may not have been based on routine imaging tests). For each eligible patient, we collected the following information: age at diagnosis, setting of diagnosis (urban or nonurban, and provincial health zone), date of first breast biopsy that confirmed DCIS or invasive breast cancer, date of first breast surgery after biopsy, definitive breast surgery type (breast conservation or mastectomy) and stage (DCIS, stage I or stage II). For the patients with stage I and II breast cancer, we additionally recorded nodal status (positive or negative), tumour grade (1, 2 or 3), presence of lymphovascular invasion (yes or no), hormone receptor (HR) status (positive or negative), human epidermal growth factor receptor 2 (HER2) status (positive or negative) and use of adjuvant radiation and/or chemotherapy.

# Imaging quantification and classification

Imaging data were obtained through both the Alberta Health Services Data Repository for Reporting (AHSDRR) diagnostic imaging database and physician billings to Alberta Health. The staging window was defined as the date of first breast biopsy confirming DCIS or invasive cancer to the first surgical date plus 4 months. We recorded the following types of diagnostic imaging tests performed during the staging window: plain chest radiograph, BS, CT, breast and nonbreast MRI, PET and nonbreast image-guided biopsy. For each imaging test, the following information was collected: anatomic region, date of test, location of test, ordering physician's specialty if available and indication for imaging as recorded on the requisition if available.

For patients with DCIS or stage I or II breast cancer who had a BS, CT, MRI or PET scan completed during

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the staging window, we reviewed the EMR to obtain test indication where not obvious from the AHSDRR Diagnostic Imaging database. For BS, CT, MRI and PET, test indication was categorized as follows: routine screening for distant metastases, screening for distant metastases on the basis of patient symptoms or signs, follow-up to a previously abnormal test, advanced breast imaging with MRI, CT or MRI angiography for planning of autologous breast reconstruction, or unrelated to breast cancer diagnosis.

# Analysis

The cohort of eligible patients was described according to patient, demographic, breast cancer and treatment characteristics. Each eligible patient was classified as having undergone routine screening for distant metastases or not. Routine screening or staging was defined as having undergone at least 1 BS, CT, MRI or PET scan in the absence of symptoms or signs concerning for metastatic disease. We did not consider the following to be routine staging tests: advanced breast imaging with MRI or CT/MRI angiography for planning of autologous reconstruction, and BS, CT, MRI or PET scanning completed for indications not related to or not obviously related to the breast cancer diagnosis. We calculated the frequency of routine staging tests by patient and number of tests. These outcomes were further evaluated by stage and type of imaging modality. As an additional end point, we calculated the frequency of preoperative chest radiography.

Patients with stage I and II breast cancer who underwent routine screening for metastases were compared with those who did not using monovariate ( $\chi^2$ ) and multivariate (logistic regression) analyses on the following variables: age group (< 40, 40–49, 50–59, 60–69, ≥ 70 yr), Charlson Comorbidity Index (CCI) score  $(0, 1, \ge 2)$ , diagnosis setting (urban, nonurban), diagnosis year (2011, 2012, 2013, 2014, 2015), type of surgery (breast conservation, mastectomy), receipt of preoperative chest radiography (no, yes), stage (I, II), tumour grade (1, 2, 3), lymphovascular invasion (no, yes), lymph node status (negative, positive), HER2 status (negative, positive) and triple-negative (estrogen receptor [ER], progesterone receptor [PR] and HER2 negative) status (no, yes). Further monovariate and multivariate sensitivity analyses were conducted. With the exclusion of patients who received neoadjuvant chemotherapy, we compared those who had routine screening with those who did not on the same variables. We also included the patients with DCIS and compared those who had routine screening with those who did not on applicable variables: age group, CCI, diagnosis setting, diagnosis year, type of surgery, receipt of preoperative chest radiography and stage.

Additionally, monovariate analysis ( $\chi^2$ ) was used to compare the frequency of patients undergoing routine screening for metastases (total and by type of imaging modality) by Choosing Wisely era. ASCO's Choosing Wisely recommendation against using advanced imaging tests for routine staging in early breast cancer was released Apr. 4, 2012. Granting time for dissemination of information, we defined the pre-Choosing Wisely era as diagnosis years 2011–2012 and the post-Choosing Wisely era as diagnosis years 2013–2015.

All statistical analyses were performed using SPSS Statistics version 19 (IBM).

# RESULTS

# Study population

Table 1 describes patient, breast cancer and treatment characteristics for the entire study population and by status of having undergone at least 1 routine staging test or not. For the entire cohort, patients had a median age at diagnosis of 60 (range 21-98) years, were healthy (CCI score of 0 in 83.3%) and most commonly received their diagnosis in an urban setting (71.1%). In terms of stage distribution, 13.8% had DCIS, 46.4% had stage I breast cancer and 39.8% had stage II breast cancer. Most of the patients with stage I and II breast cancer had ER-positive (87.7%) and HER2-negative (87.4%) disease. The frequency of breast-conserving surgery (55.8%) was similar to that for adjuvant radiation (56.2%), while only 32.7% had chemotherapy (28% adjuvant and 4.7% neoadjuvant). Patients who underwent at least 1 routine staging test tended to be younger, were more often diagnosed in a nonurban setting and had breast cancer characteristics as follows: higher stage, lymph node positive, higher grade, presence of lymphovascular invasion (LVI), HER2 positive and triple negative. Furthermore, screened patients had a higher frequency of also having undergone preoperative chest radiography and were more likely to be treated with mastectomy, radiation and chemotherapy.

# Use of advanced imaging tests for routine metastatic screening

Figure 1 outlines how patients who underwent routine imaging tests to screen for metastatic disease were identified. In the study period, 10 142 patients underwent breast surgery for management of DCIS or stage I or stage II breast cancer. For this cohort, 6321 advanced imaging tests (BS, CT, MRI or PET) were identified during the staging window among 3845 patients. Of these advanced imaging tests, 1437 were excluded for the following reasons: advanced breast imaging with MRI (173); CT/MRI angiography for planning of autologous reconstruction (50); BS, CT, MRI or PET scanning completed for an indication not related to the breast cancer diagnosis (1185); and CT scanning completed for reasons unknown (29). Furthermore, 651 tests were excluded as the patient

	attent, breast cancel all	a treatment characteristics of	study popu	
	No. (%) of patients;* receipt of imaging test			No. (%) of patients
Characteristic	Routine BS, CT, MRI or PET $n = 2887$	No routine BS, CT, MRI or PET $n = 7255$	p value	Entire cohort $n = 10\ 142$
Age group, yr			< 0.001	
≤ 40	234 (8.1)	273 (3.8)		507 (5.0)
41–50	550 (19.1)	1107 (15.3)		1657 (16.3)
51–60	773 (26.8)	1915 (26.4)		2688 (26.5)
61–70	737 (25.5	1982 (27.3)		2719 (26.8)
> 70	593 (20.5)	1978 (27.3)		2571 (25.4)
CCI score			0.476	
0	2420 (84.0)	5971 (83.1)		8391 (83.3)
1	342 (11.9)	915 (12.7)		1257 (12.5)
> 2	118 (4.1)	302 (4.2)		420 (4.2)
Unknown no	7	67		74
Year of diagnosis	1	57	0.008	7.4
2011	567 (19.6)	1317 (18.2)	0.000	1884 (18.6)
2011	554 (19.2)	1370 (18.9)		1924 (19.0)
2013	529 (18 2)	1/152 (20 0)		1921 (19 5)
2014	654 (22 7)	1497 (20.0)		2151 (21 2)
2015	583 (20 2)	1619 (22 3)		2101 (21.2)
Zone at diagnosis†	303 (20.2)	1013 (22.3)	< 0.001	2202 (21.7)
71	602 (20 9)	2740 (27.9)	< 0.001	22/12 (22 0)
72	1102 (41.2)	2740 (37.8)		2060 (20 1)
72	451 (15 G)	2070 (30.3)		
74	402 (14.0)	962 (11.0)		1265 (12.5)
75	229 (9.2)	625 (9.9)		972 (9.6)
20 Sotting of diagnosis	230 (0.2)	033 (6.8)	< 0.001	073 (0.0)
	1705 (62.0)	E 41 C /7 A 7)	< 0.001	7011 (71 1)
Dural	1795 (62.2)	1820 (25.2)		/211(/1.1)
	1092 (37.8)	1839 (25.3)	0.001	2931 (28.9)
radiograph			< 0.001	
Yes	988 (34.2)	1926 (26.5)		2914 (28.7)
No	1899 (65.8)	5329 (73.5)		7228 (71.3)
Surgery			< 0.001	
Mastectomy	1612 (55.9)	2869 (39.6)		4481 (44.2)
BCS	1274 (44.1)	4382 (60.4)		5656 (55.8)
Unknown, no.	1	4		5
Stage			< 0.001	
0 (DCIS)	52 (1.8)	1345 (18.5)		1397 (13.8)
I	759 (26.3)	3949 (54.4)		4708 (46.4)
11	2076 (71.9)	1961 (27.0)		4037 (39.8)
Lymph dode			< 0.001	
Positive	1310 (48.3)	598 (8.6)		1908 (19.8)
Negative	1401 (51.7)	6351 (91.4)		7752 (80.2)
Unknown, no.	176	306		482
Grade			< 0.001	
	347 (12.2)	1459 (21.2)		1806 (18.6)
2	1190 (41.8)	2921 (42.5)		4111 (42.3)
3	1307 (46.0)	2490 (36.2)		3797 (39.1)
Unknown, no.	43	385		428
VI			< 0.001	
Present	1002 (36.5)	109615.4)		2098 (21.3)
Absent	1745 (63.5)	6002 (84.6)		7747 (78.7)
Unknown, no.	140	157		297
ER status			< 0.001	
Positive	2443 (85.3)	5834 (88 8)		8277 (87 7)
Negative	Δ22 (1Δ 7)	736 (11.2)		1158 (12 3)
Unknown no	22 (17.7)	685		707
Shikhovin, no.	<u> </u>	000		/0/

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Table 1 (part 2 of 2). Patient, breast cancer and treatment characteristics of study population				
	No. (%) of patients;*		No. (%) of patients	
Characteristic	Routine BS, CT, MRI or PET n = 2887	No routine BS, CT, MRI or PET n = 7255	p value	Entire cohort $n = 10\ 142$
PR status			< 0.001	
Positive	2127 (74.2)	5113 (77.9)		7240 (76.8)
Negative	738 (25.8)	1449 (22.1)		2187 (23.2)
Unknown, no.	22	693		715
HER2 status			< 0.001	
Positive	459 (16.5)	621 (10.7)		1080 (12.6)
Negative	2319 (83.5)	5159 (89.3)		7478 (87.4)
Unknown, no.	109	1475		1584
TNBC			0.006	
Yes	262 (9.4)	444 (7.7)		706 (8.3)
No	2516 (90.6)	5331 (92.3)		7847 (91.7)
Unknown, no.	109	1480		1589
Chemotherapy			< 0.001	
Yes	1685 (58.4)	1635 (22.5)		3320 (32.7)
No	1202 (41.6)	5620 (77.5)		6822 (67.3)
Radiotherapy			< 0.001	
Yes	1723 (59.7)	3980 (54.9)		5703 (56.2)
No	1164 (40.3)	3275 (45.1)		4439 (43.8)

BCS = breast-conserving surgery; BS = bone scanning; CCI = Charlson Comorbidity Index; CT = computed tomography; DCIS = ductal carcinoma in situ; ER = estrogen receptor; HER2 = human epidermal growth factor receptor 2; LVI = lymphovascular invasion; MRI = magnetic resonance imaging; PET = positron emission tomography; PR = progesterone receptor; TNBC = triple-negative breast cancer.

\*Unless indicated otherwise.

†Alberta Health Services is organized into 5 geographic zones.



**Fig. 1.** Study flow chart. BS = bone scan; CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

was reported to have symptoms or signs worrisome for distant disease. These 651 tests were among 541 patients, meaning that 5.2% of the patients in our study cohort underwent screening for metastatic disease for a potentially valid reason. Finally, 546 tests were excluded because of categorization as a follow-up test. This left 3687 tests having been completed for routine staging among 2887 patients. Hence, the incidence of patients who underwent routine screening for metastases was 28.5%, and the mean number of tests per patient was 1.3 (standard deviation 0.5). The incidence of routine screening was 3.7% among patients with DCIS, 16.1% among those with stage I breast cancer and 51.4% among those with stage II breast cancer (Table 2). Patients were most commonly subjected to BS, followed by CT and then PET; none of our patients had an MRI for routine screening (Table 2). Of the 2887 patients who underwent routine screening, 546 follow-up tests (most commonly CT and MRI) were completed during the staging window among 438 patients (15.2%). Furthermore, we identified 28 patients who underwent a nonbreast image-guided biopsy (1.0%).

# Monovariate and multivariate analyses

For patients with stage I and II breast cancer, monovariate and multivariate analyses revealed significant associations between the following variables and routine staging: age  $(\geq 70 \text{ yr relative to younger age groups})$ , year of diagnosis (2011 relative to 2013 and 2015 but not relative to 2012 or 2014), setting of diagnosis (nonurban relative to urban), type of surgery (mastectomy relative to breast-conserving surgery), stage (II relative to I), lymph node status (positive relative to negative), grade (2 and 3 relative to 1) and HER2 status (positive relative to negative) (Table 3). Preoperative chest radiography (yes relative to no), LVI (positive relative to negative) and triple-negative status (yes v. no) were significantly associated with routine staging with monovariate analysis only, while CCI score was not associated with routine staging using monovariate or multivariate analysis (Table 3). Exclusion of patients who received neoadjuvant treatment did not change the results of the monovariate and multivariate analyses. With inclusion of patients with DCIS, significant associations with routine staging persisted for the applicable variables (age, year of diagnosis, setting of diagnosis, type of surgery and stage).

# Pre- versus post-Choosing Wisely eras

In a further exploratory analysis, we investigated the influence of Choosing Wisely era on the use of routine staging with BS, CT and PET. Overall, total use of BS, CT and PET was unchanged between the pre- and post-Choosing Wisely eras (Fig. 2). For the separate routine imaging modalities considered, utilization of CT significantly increased (7.5% pre-Choosing Wisely era v. 10.8% post-Choosing Wisely era, p < 0.001).

# DISCUSSION

To our knowledge, we have presented the first provincial, population-based study to report on the use of advanced imaging tests for routine investigation of metastases among women diagnosed with DCIS or stage I or stage II breast cancer during an era that spanned the release of ASCO's Choosing Wisely recommendations. Of 10142 patients who had received a diagnosis in the years 2011 through 2015, 2886 (28.5%) had at least 1 BS, CT or PET completed for routine staging purposes between the date of first breast biopsy confirming DCIS or invasive cancer and the first surgical date plus 4 months. Bone scanning was the most frequently ordered modality followed by CT and then PET; MRI was not used for routine staging purposes. Of the 2886 patients who had an advanced imaging test for routine staging, 438 (15.2%) had a follow-up BS, CT, MRI or PET, and 28 (1.0%) had a nonbreast imageguided biopsy within the staging window.

Simos and colleagues reported on the use of plain radiography, ultrasonography, BS, CT and MRI for routine staging among patients with stage I or II breast cancer in the years 2007 through 2012 in Ontario.<sup>20</sup> In their provincial cohort, 85.9% of patients underwent at least 1 of these tests. Considering the initial advanced imaging tests completed for patients with stage I or II breast cancer in the final year of the Ontario cohort, we can make some comparisons with our Alberta cohort (Fig. 2 in Simos and colleagues and Table 2 in our study). In both cohorts, BS was used more than CT. Their use of BS appeared higher

Table 2. Routine staging tests completed, by stage and imaging modality					
	No. (%) of patients who underwent imaging; imaging modality				
Stage	BS	СТ	MRI	PET	Total
DCIS, <i>n</i> = 1397	36 (2.6)	20 (1.4)	0 (0)	0 (0)	52 (3.7)
l, <i>n</i> = 4708	661 (14.0)	207 (4.4)	0 (0)	6 (0.1)	759 (16.1)
II, <i>n</i> = 4037	1880 (46.6)	746 (18.5)	0 (0)	12 (0.3)	1961 (51.4)
BS = bone scanning; CT = computed tomography; DCIS = ductal carcinoma in situ; MRI = magnetic resonance imaging; PET = positron emission tomography.					

Table 3. Monovariate and imaging and positron em	I multivariate analyses of use of ission tomography in patients v	routine bone scann vith stage I and II br	ing, computed tomography, ma east cancer	gnetic resonance
	Monovariate an	alysis	Multivariate a	nalysis
Variable	OR (95%CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Age group, yr				
≥ 70	Ref		Ref	
60–69	1.240 (1.095–1.405)	0.001	1.206 (1.029–1.412)	0.020
50–59	1.346 (1.189–1.524)	< 0.001	1.267 (1.081–1.485)	0.004
40–49	1.657 (1.445–1.901)	< 0.001	1.379 (1.154–1.648)	< 0.001
< 40	2.859 (2.347–3.482)	< 0.001	1.551 (1.202–2.002)	0.001
CCI score				
0	Ref		Ref	
1	0.922 (0.807–1.053)	0.232	0.891 (0.752–1.055)	0.18
≥ 2	0.964 (0.775–1.199)	0.742	0.807 (0.609–1.070)	0.14
Year of diagnosis				
2011	Ref		Ref	
2012	0.939 (0.817–1.080)	0.378	0.886 (0.743–1.058)	0.18
2013	0.846 (0.736–0.973)	0.019	0.821 (0.687–0.980)	0.029
2014	1.015 (0.887–1.161)	0.831	1.011 (0.852–1.199)	0.90
2015	0.836 (0.730–0.959)	0.010	0.729 (0.612–0.868)	< 0.001
Setting of diagnosis				
Urban	Ref		Ref	
Rural	1.792 (1.634–1.964)	< 0.001	2.107 (1.871–2.372)	< 0.001
Surgery				
Mastectomy	Ref		Ref	
BCS	0.517 (0.474–0.565)	< 0.001	0.687 (0.614–0.768)	< 0.001
Stage				
0 (DCIS)	NA		NA	
	Ref	Ref		
	5.508 (4.988–6.083)	< 0.001	2.254 (1.963–2.588)	< 0.001
Lymph node status				
Negative	Ref		Ref	
Positive	9.931 (8.872–11.115	< 0.001	4.763 (4.094–5.541)	< 0.001
Grade				
	Ref		Ref	
2	1.713 (1.496–1.961	< 0.001	1.343 (1.141–1.581)	< 0.001
3	2.207 (1.929–2.526	< 0.001	1.569 (1.308–1.883)	< 0.001
LVI				
Absent	Ref		Ref	
Present	3.145 (2.843–3.478	< 0.001	1.035 (0.905–1.183)	0.62
HER2 status				
Negative	Ref		Ref	
Positive	1.644 (1.444–1.873	< 0.001	1.248 (1.051–1.483)	0.012
TNBC				
No	Ref		Ref	
Yes	1.250 (1.066–1.467	0.006	1.110 (0.903–1.364)	0.32
BCS = breast-conserving surgery; C	CI = Charlson Comorbidity Index: CI = confide	ence interval: DCIS = ductal	carcinoma in situ: HER2 = human epidermal q	rowth factor receptor 2:   VI =

BCS = breast-conserving surgery; CCI = Charlson Comorbidity Index; CI = confidence interval; DCIS = ductal carcinoma in situ; HER2 = human epidermal growth factor receptor 2; LVI = lymphovascular invasion; NA = not applicable; OR = odds ratio; Ref = reference category; TNBC = triple-negative breast cancer.

for patients with stage I breast cancer (around 30% in 2012 in Ontario v. 14% in all years in Alberta) and for patients with stage II breast cancer (around 55% in 2012 in Ontario v. 46.6% in all years in Alberta). Their use of CT appeared only slightly higher for patients with stage I breast cancer (around 8% in 2012 in Ontario v. 4.4% in all years in Alberta) and for patients with stage II breast cancer (around 20% in 2012 in Ontario v. 18.5% in all

years in Alberta). The finding that higher proportions of patients with stage I and II breast cancer underwent BS and CT in Ontario could be explained by potential inclusion of symptomatic patients and patients undergoing tests for other reasons (such patients were excluded from our study), differences in staging guidelines (the Ontario guideline included BS for patients with stage II breast cancer<sup>6</sup> but the Alberta guideline removed it for these



**Fig. 2.** Use of routine BS, CT and PET before and after the release of the American Society of Clinical Oncology's Choosing Wisely recommendations. BS = bone scan; CT = computed tomography; PET = positron emission tomography.

patients in 2012<sup>8</sup>), and the timing of the cohort in relation to the release of the ASCO Choosing Wisely recommendations. The timing of the cohort seems to be a less likely explanation as Simos and colleagues reported that although the proportion of women subjected to routine imaging for staging purposes remained relatively stable over time, the use of conventional tests (plain radiography, ultrasonography) decreased, and the use of some advanced tests (CT, MRI) increased. Our study also found a small but significant increase in the use of CT and overall no change in the use of advanced imaging tests before versus after the release of the ASCO Choosing Wisely recommendatoins.

The potential impact of ASCO's Choosing Wisely recommendations has been examined in other studies. A single institution in Ontario examined the records of 100 consecutive patients with breast cancer seen in 2011 and 100 consecutive patients with breast cancer seen in September to November 2012.<sup>25</sup> The proportion of patients undergoing at least 1 staging test not concordant with the ASCO recommendations was 77% in 2011 and 75% in late 2012, suggesting that there had been no immediate change in practice as a result of the release of the recommendations.

In the United States, adherence to the ASCO recommendation against routine BS, CT or PET for asymptomatic patients with stage 0–II breast cancer may be better. Similar to our study, Henry and colleagues included patients with DCIS and stage I and II breast cancer over a time period spanning the release of the ASCO recommendations.<sup>26</sup> Among 34 078 patients who received a diagnosis from 2008 through 2015 in 25 hospital systems included in the Michigan Breast Oncology Quality Initiative, 20.1% underwent BS, CT or PET within 3 months of diagnosis. The proportion tested significantly decreased over time for patients with DCIS, stage I and stage IIA disease; however, the proportion tested remained stable for patients with stage IIB breast cancer. The reason for each imaging test was abstracted for patients who received a diagnosis in 2014 and 2015. Notably, in just over half of those tested, the reason was considered valid. Ramsey and colleagues used data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program and linked Premera Blue Cross claims data for patients with cancer diagnosed in western Washington State between 2007 and 2014.27 Among 1798 patients with stage 0-II breast cancer, 22% underwent BS, CT or PET. Rocque and colleagues conducted a retrospective analysis of Medicare claims data for patients with cancer diagnosed in the University of Alabama at Birmingham Health System Cancer Community Network for a time period that largely followed the release of ASCO's Top Five list (2012–2015).<sup>28</sup> They included 6675 patients with breast cancer and found that only 11.6% of those with stage 0-II disease underwent BS, CT or PET. For the cohorts in the studies by Ramsey and colleagues and Rocque and

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colleagues, the reason for BS, CT or PET was not obtained and hence the proportions of women undergoing unnecessary staging may have actually been lower.

The apparent greater use of advanced imaging tests for staging among patient with early breast cancer in Canadian relative to US cohorts could be related to both a lack of insurer oversight and a delay in widespread guideline dissemination and/or adoption in Canada. In a survey of a small sample of Canadian breast cancer physicians, although 82% indicated awareness of at least 1 published breast cancer staging guideline, only 60% indicated that they had read the ASCO Top Five list and were aware of the specific recommendation against performing routine staging tests for asymptomatic women with stage 0-II breast cancer.<sup>29</sup> Of note, in our study, patients were more likely to undergo routine BS, CT, PET, MRI or PET if they also had a preoperative chest radiograph. Likewise, in response to the ABIM Choosing Wisely Campaign, on Apr. 4, 2012, the American College of Radiology recommended against preoperative chest radiography for ambulatory patients with unremarkable history and physical.<sup>30</sup> This recommendation was subsequently endorsed by the American College of Surgeons on Sept. 4, 2013,<sup>31</sup> and by Choosing Wisely Canada (General Surgery) on Apr. 2, 2014.32

Guideline dissemination and adoption is probably also related to the specifics of local practice, as in our study and others there was significant variation in the use of routine staging tests by region (i.e., urban v. rural) and/or type of hospital (i.e., academic v. community).<sup>20,26,28</sup> Although strategies to improve guideline diffusion and implementation of rules for reimbursement could aid with adherence to staging recommendations, physicians may continue to be swayed by details of the clinical scenario. In our study and others, physicians were more likely to order staging tests according to patient and breast cancer pathologic characteristics potentially associated with a higher risk of recurrence and in patients treated more aggressively (i.e., mastectomy for type of surgery).<sup>20,26</sup> Although higher T stage and N stage are also associated with higher risk of metastases at diagnoses,<sup>6,33,34</sup> this association has not been confirmed for other factors such as younger patient age, higher tumour grade, HER2-positive disease and triple negative-disease.<sup>34</sup> However, further research on the risk of metastases at diagnosis by breast cancer subtype is probably warranted, especially for stage IIB disease, where PET has been found to identify metastases in 10.7% of patients.<sup>34</sup>

Overall, our findings represent the use of BS, CT, nonbreast MRI and PET for routine staging of patients with DCIS and stage I and stage II breast cancer for a single province in a timeframe that spanned the publication of ASCO's Choosing Wisely recommendations. Ascertainment of our cohort was largely unbiased given that we identified eligible patients from the provincial registry. There was minimal risk for misclassification of patients by stage in that only 473 patients (4.7%) had neoadjuvant chemotherapy and may have experienced downstaging before surgery. Further, exclusion of these patients in monvariate and multivariate analyses did not affect the results.

# Limitations

To report on advanced imaging tests done unnecessarily for metastastic screening, we examined the indication on the imaging requisition and as per notes in the EMR where necessary. Only 29 tests (0.5%) were ordered for unknown reasons. However, we acknowledge that classification of test reason may be associated with some degree of error because the data were reviewed retrospectively. Another limitation is that we could not reliably or completely identify the specialty of the physician ordering BS, CT, MRI or PET. Hence, we could not examine ordering physician specialty in our monovariate and multivariate analyses. Such information may have been useful for knowledge translation. Further, while documentation of unnecessary staging tests implies wasted resources and the prospect for reallocation to areas of need, we have not provided an economic analysis for our setting as others have done in similar studies.<sup>16,26-28</sup> Finally, we have not yet compared patients who had unnecessary staging tests with those who did not in terms of important outcomes such as use of psychosocial services, time to adjuvant treatment(s) and follow-up imaging tests completed beyond the staging window.

# CONCLUSION

Almost 30% of patients with DCIS or stage I or stage II breast cancer diagnosed between 2011 and 2015 in Alberta had at least 1 advanced imaging test completed for routine staging purposes. Despite the release of the ASCO Choosing Wisely recommendations, the utilization of BS, CT and PET did not decrease during the study period. There is an opportunity to improve the quality and value of the care provided to women with early breast cancer, and it is clear that strategies beyond guideline publication are required.

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# References

- Canadian Cancer Statistics Advisory Committee. *Canadian cancer statistics 2018*. Toronto (ON): Canadian Cancer Society; 2018. Available: cancer.ca/Canadian-Cancer-Statistics-2018-EN (accessed 2019 Jan. 22).
- 2. Canadian Partnership Against Cancer. *Breast cancer control in Canada: a system performance special focus report.* Toronto (ON): Canadian Partnership Against Cancer; 2012.
- Surveillance & Reporting. The 2017 report on cancer statistics in Alberta. Edmonton: Alberta Health Services; 2017. Available: public. tableau.com/views/The2017ReportonCancerStatisticsinAlberta/ Highlights?:showVizHome=no (accessed 2019 Jan. 22).
- 4. Goulart BHL. Value: the next frontier in cancer care. *Oncologist* 2016;21:651-3.
- Tran K, Rahal R, Fung S, et al. Choosing wisely in cancer control across Canada — a set of baseline indicators. *Curr Oncol* 2017; 24:201-6.
- Myers RE, Johnston M, Pritchard K, et al; Breast Cancer Disease Site Group of the Cancer Care Ontario Practice Guidelines Initiative. Baseline staging tests in primary breast cancer: a practice guideline. *CMAJ* 2001;164:1439-44.
- Eastern Health. Cancer care clinical practice guidelines. Staging of primary breast cancer. St. John's (NL): Eastern Health; 2011. Available: www. easternhealth.ca/WebInWeb.aspx?d=4&id=1516&p=1495 (accessed 2019 Jan. 22).
- Alberta Health Services. Staging investigations for asymptomatic and newly diagnosed breast cancer. Clinical practice guideline BR-012 version 2. Edmonton: Alberta Health Services; 2012. Available: www. albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide -br012-staging-investigations.pdf (accessed 2019 Jan. 22).
- National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology. Breast cancer version 1. Plymouth Meeting (PA): National Comprehensive Cancer Network; 2014. Available: www.nccn.org/professionals/physician\_gls/pdf/breast.pdf (accessed 2019 Jan. 22).
- Senkus E, Kyriakides S, Penault-Llorca F, et al. Primary breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2013;24(Suppl 6):vi7-23.
- Ravaioli A, Tassinari B, Pasini G, et al. Staging of breast cancer: What standards should be used in research and clinical practice? *Ann Oncol* 1998;9:1173-7.
- Puglisi F, Follador A, Minisini AM, et al. Baseline staging tests after a new diagnosis of breast cancer: further evidence of their limited indications. *Ann Oncol* 2005;16:263-6.
- Brennan ME. Houssami. Evaluation of the evidence on staging imaging for detection of asymptomatic distant metastases in newly diagnosed breast cancer. *Breast* 2012;21:112-23.
- Rayson D, Porter G. Investigations for patients with early-stage breast cancer: oversetting the stage. CMA7 2015;187:860-1.
- Dinan MA, Curtis LH, Hammill BG, et al. Changes in the use and costs of diagnostic imaging among Medicare beneficiaries with cancer, 1996–2006. *JAMA* 2010;303:1625-31.
- Thavorn K, Wang Z, Fergusson D, et al. Cost implications of unwarranted imaging for distant metastasis in women with earlystage breast cancer in Ontario. *Curr Oncol* 2016;23(S1):S52-5.
- Crivello ML, Ruth K, Sigurdson ER, et al. Advanced imaging modalities in early stage breast cancer: preoperative use in the United States Medicare population. *Ann Surg Oncol* 2013;20:102-10.

- Markov DV, Soulos PR, Gold HT, et al. Regional-level correlations in inappropriate imaging rates for prostate and breast cancers: potential implications for the Choosing Wisely Campaign. *JAMA Oncol* 2015;1:185-94.
- Linkugel A, Margenthaler J, Dull B, et al. Staging studies have limited utility for newly diagnosed stage I-II breast cancer. *J Surg Res* 2015;196:33-8.
- Simos D, Catley C, van Walraven C, et al. Imaging for distant metastases in women with early-stage breast cancer: a population based cohort study. CMA7 2015;187:E387-97.
- Kamal A, Zhang T, Power S, et al. Is advanced imaging in early stage breast cancer ever warranted? Reconciling clinical judgement with common quality measures. *J Natl Compr Canc Netw* 2016;14:993-8.
- 22. Dull B, Linkugel BA, Margenthaler JA, et al. Overuse of CT chest in patients with stage I and II breast cancer: an opportunity to increase guidelines compliance at an NCCN member institution. *J Natl Compr Canc Netw* 2017;15:783-9.
- Schnipper LE, Smith TJ, Raghavan D, et al. American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: the top five list for oncology. *J Clin Oncol* 2012;30:1715-24.
- 24. Edge SB, Byrd DR, Compton CC, et al., editors. *AJCC cancer staging manual*. 7th ed. New York: Springer; 2010.
- Simos D, Hutton B, Clemons M. Are physicians choosing wisely when imaging for distant metastases in women with operable breast cancer? *J Oncol Pract* 2014;11:62-71.
- Henry NL, Braun TM, Breslin TM, et al. Variation in the use of advanced imaging at the time of breast cancer diagnosis in a statewide registry. *Cancer* 2017;123:2975-83.
- 27. Ramsey SD, Fedorenko C, Chauhan R, et al. Baseline estimates of adherence to American Society of Clinical Oncology/American Board of Internal Medicine Choosing Wisely Initiative among patients with cancer enrolled with a large regional commercial health insurer. *J Oncol Pract* 2015;11:338-44.
- Rocque GB, Williams CP, Jackson BE, et al. Choosing Wisely: Opportunities for improving value in cancer care delivery? *J Oncol Pract* 2017;13:e11-21.
- Simos D, Hutton B, Graham ID, et al. Imaging for metastatic disease in patients with newly diagnosed breast cancer: are doctor's perceptions in keeping with the guidelines? *J Eval Clin Pract* 2015;21:67-73.
- Choosing Wisely, American College of Radiology. *Ten things physicians and patients should question*. Philadelphia: American Board of Internal Medicine Foundation; 2012. Available: www.choosingwisely. org/wp-content/uploads/2015/02/ACR-Choosing-Wisely-List.pdf (accessed 2019 Jan. 22).
- Choosing Wisely, American College of Surgeons. *Five things physicians and patients should question*. Philadelphia: American Board of Internal Medicine Foundation; 2013. Available: www.choosingwisely. org/societies/american-college-of-surgeons/ (accessed 2019 Jan. 22).
- Canadian Association of General Surgeons. General surgery. Six things physicians and patients should question. Choosing Wisely Canada; 2014. Available: https://choosingwiselycanada.org/general-surgery/ (accessed 2019 Jan. 22).
- Tanaka S, Sato N, Fujioka H, et al. Use of contrast-enhanced computed tomography in clinical staging of asymptomatic breast cancer patients to detect asymptomatic distant metastases. *Oncol Lett* 2012;3:772-6.
- 34. Groheux D, Hindie E, Delord M, et al. Prognostic impact of 18FDG-PET-CT findings in clinical stage III and IIB breast cancer. *J Natl Cancer Inst* 2012;104:1879-87.