



EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Directorate F - Health, Consumers & Reference Materials (Ispra)
Health in Society

European Commission Initiative on Breast Cancer (ECIBC): European guidelines on breast cancer screening and diagnosis

QUESTION

Should conventional staging exams vs. no staging exams be used for patients with clinical stage I breast cancer without symptoms suggestive of metastases?

POPULATION:	patients with clinical stage I breast cancer without symptoms suggestive of metastases
INTERVENTION:	conventional staging exams
COMPARISON:	no staging exams
MAIN OUTCOMES:	Detection rate: Combined tests (prevalence); False Positive: Combined tests; Detection rate: Bone Scan; False positive: Bone Scan; Detection rate: TC chest; False positive: TC chest; Detection rate: CT Pelvic ; False positive: CT Pelvic; Detection rate: TC abdominal; False positive: TC abdominal; Detection rate: Chest X-Ray; False positive: Chest X-Ray; Detection rate: US; False positive: US;
SETTING:	European Union
PERSPECTIVE:	Population (National Health System)
BACKGROUND:	The main cause of death from breast cancer is due to distant metastases. The detection of distant metastases in patients with newly diagnosed breast cancer alters treatment and prognosis. If metastases are present, the prognosis worsens significantly and the treatment has to balance between prolongation of survival and quality of life since the disease is no longer curable. Therefore, the staging interventions aim to avoid overtreatment in patients with primarily metastasized breast cancer and, in some cases, to start treatments that are specific for metastases. However, the risk for metastases is lower in early detected (clinical stage I and II) breast cancer than in later stages (clinical stage III). Although, the staging interventions have the advantage of ensuring adequate treatment adapted to the tumour stage, they are also associated with some disadvantages like limited specificity, leading to false positive with consequent psychological stress for the women, unnecessary ascertainment and, when ascertainment is not possible leading to wrong treatment planning; furthermore some imaging techniques have procedure related consequences, in particular radiation (depending on the used technique) and high costs.
CONFLICT OF INTEREST:	<p>ColS for all Guidelines Development Group (GDG) members were assessed and managed by the European Commission Joint Research Centre (JRC) following an established procedure in line with the institutional rules. GDG member participation in the development of the recommendations was restricted, according to CoI disclosure. Consequently, for this particular question, the following GDG members were recused from voting: Axel Gräwingholt. Miranda Langendam, as external expert, was also not allowed to vote, according to the ECIBC rules of procedure.</p> <p>For more information please visit: http://ecibc.jrc.ec.europa.eu/gdg-documents</p>

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know 	<p>The detection of distant metastases in patients with newly diagnosed breast cancer alters treatment and prognosis. If metastases are present, the prognosis worsens significantly and the treatment has to balance between prolongation of survival and quality of life since the disease is no longer curable. Therefore, the staging interventions aim to avoid overtreatment in patients with primarily metastasized breast cancer and, in some cases, to start treatments that are specific for metastases.</p> <p>Although, the staging interventions have the advantage of ensuring adequate treatment adapted to the tumour stage, they are also associated with some disadvantages like limited specificity, leading to false positive with consequent psychological stress for the women, unnecessary ascertainment and, when ascertainment is not possible leading to wrong treatment planning; furthermore some imaging techniques have procedure related consequences, in particular radiation (depending on the used technique) and high costs.</p>	<p>The GDG prioritised this question for the ECIBC.</p>

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">● Trivial○ Small○ Moderate○ Large○ Varies○ Don't know	Outcomes	Impact	No of participants (studies)	Certainty of the evidence (GRADE)	Sensitivity analysis without Puglisi (2005): *Pooled detection rate: 1 per 1,000 examinations (95% CI: 0 - 8); n/N = 3/1722 (4 studies) In one study including 411 clinical stage II breast cancer patients (Bychkovsky BL, 2006) evaluated by conventional imaging, the percentage of distant metastases did not differ by BC subtype: among ER/PR-positive and HER2-negative patients was 2.2% (95% CI, 0.5%–6.4%), for HER2+ patients was 1.9% (95% CI, 0%–9.9%), and in TNBC patients was 2.1% (95% CI, 0.1%–11.1%). Another study in 254 patients with BC clinical stage II and III evaluated by 18FDG-PET-CT (Groheux D, 2012), reported that the rates of distant metastases did not differ between TNBC (16 %), HER2- positive (26 %), and ER-positive (22 %) breast cancers subtypes (p =0.42). It must be kept in mind that these two studies do not include clinical stage I breast cancer patients, and the evidence is indirect. The GDG judged by
	Detection rate: Combined tests (prevalence)	Pooled detection rate: 8 per 1,000 examinations (95% CI: 0 - 30); n/N = 15/1,958	(5 RCTs) ^{1,2,3,4,5}	⊕⊕○○ LOW ^{a,b,c,d}	
	Detection rate: Bone Scan	Pooled detection rate: 5 per 1,000 examinations (95% CI 0 - 21) n/N = 17/2,397	(5 RCTs) ^{1,2,4,6,7}	⊕⊕○○ LOW ^{a,b,d,e}	
	Detection rate: TC chest	Pooled detection rate: 0 per 1,000 examinations (95% CI: 0 - 5) n/N = 2/485	(2 RCTs) ^{1,8}	⊕⊕○○ LOW ^{a,b,d,e}	
	Detection rate: CT Pelvic	Detection rate: 31 per 1,000 examinations (95% CI: 7.3 - 92.1); n/N = 1/32	(1 RCT) ¹	⊕○○○ VERY LOW ^{a,b,d,e,f}	

Detection rate: TC abdominal	Detection rate: 23 per 1,000 examinations (95% CI: 7.3 - 92.1); n/N = 1/43	(1 RCT) ¹	⊕○○○ VERY LOW ^{a,b,d,e,f}
Detection rate: Chest X-Ray	Pooled detection rate: 0 per 1,000 examinations (95% CI: 0 - 2); n/N = 0/1,049	(3 RCTs) ^{1,2,5}	⊕⊕○○ LOW ^{a,b,d,e}
Detection rate: US	Pooled detection rate: 0 per 1000 examinations (95% CI: 0 - 11); n/N = 1/407	(3 RCTs) ^{1,2,4}	⊕⊕⊕○ MODERATE ^{a,b,e}

consensus that the desirable effects were trivial.

1. Dillman RO, Chico S.. Radiologic tests after a new diagnosis of breast cancer.. Eff Clin Pract.; 2000.
 2. Puglisi F, Follador A, Minisini AM, Cardellino GG, Russo S, Andreetta C, Di Terlizzi S, Piga A.. Baseline staging tests after a new diagnosis of breast cancer: further evidence of their limited indications.. Ann Oncol.; 2005.
 3. Ravaioli A, Tassinari D, Pasini G, Polsell A, Papi M, Fattori PP, Pasquini E, Masi A, Alessandrini F, Canuti D, Panzini I, Drudi G.. Staging of breast cancer: what standards should be used in research and clinical practice?. Ann Oncol. ; 1998.
 4. Kasem AR, Desai A, Daniell S, Sinha P.. Bone scan and liver ultrasound scan in the preoperative staging for primary breast cancer.. Breast J. ; 2006.
 5. Barret T, Bowden DJ, Greenberg DC, Brown CH, Wishart PD. Radiological staging in breast cancer: which asymptomatic patients to image and how. Br J Cancer; 2009.
 6. Lee JE, Park SS, Han W, Kim SW, Shin HJ, Choe KJ, Oh SK, Youn YK, Noh DY, Kim SW.. The clinical use of staging bone scan in patients with breast carcinoma: reevaluation by the 2003 American Joint Committee on Cancer staging system.. Cancer. ; 2005.
 7. Koizumi M, Yoshimoto M, Kasumi F, Ogata E.. What do breast cancer patients benefit from staging bone scintigraphy?. Jpn J Clin Oncol.; 2001.
 8. Kim H, Han W, Moon HG, Min J, Ahn SK, Kim TY, Im SA, Oh DY, Han SW, Chie EK, Ha SW, Noh DY.. The value of preoperative staging chest computed tomography to detect asymptomatic lung and liver metastasis in patients with primary breast carcinoma.. Breast Cancer Res Treat.; 2011.
- a. Different reference standards were used, some included another imaging test without histological confirmation which is likely to incorrectly classify the condition
 - b. Some studies included retrospective case records where inclusion criteria cannot be properly assessed, in some cases the distribution of stages at diagnosis is not that expected in the population, in particular stage I and stage II are under-represented; this suggest that only a subpopulation of these cases entered in the study and that they could be those with higher suspicious of having distal metastases.
 - c. The proportion of patients actually staging investigated with more than one imaging tests was variable which could underestimated the exams' performance. All studies reported to include follow-up of patients although with different time frame.
 - d. Some or most of the studies recruited consecutive patients from medical records (or prospectively) which could or could not have symptoms suggestive of metastases.
 - e. The assessment of each individual tests is based in the number of patients that were examined who are a subpopulation of all those subject at this stage which could overestimate its performance measurements.
 - f. Judgement of imprecision was considered serious as one or both of the confidence interval limits reached detection rates threshold which could potentially change the decision about requesting staging tests.

Outcomes	Impact	Nº of participants (studies)	Certainty of the evidence (GRADE)
False Positive: Combined tests (prevalence)	Pooled false positive: 49 per 1,000 examinations (95% CI: 4 - 131); n/N = 29/1,220	(3 RCTs) ^{1,2,3}	⊕⊕○○ LOW ^{a,b,c,d}
False positive: Bone Scan	False positive: 164 per 1,000 examinations (95% CI: 91.6 - 276.1); n/N = 10/61	(1 RCT) ²	⊕⊕○○ LOW ^{a,b,e,f}
False positive: TC chest	False positive: 134 per 1,000 examinations (95% CI: 106 - 169); n/N = 60/448	(1 RCT) ⁴	⊕⊕○○ LOW ^{a,b,e,f}
False positive: CT Pelvic - not reported		-	-
False positive: TC abdominal - not reported		-	-
False positive: Chest X-Ray - not reported		-	-
False positive: US	False positive: 16 per 1,000 examinations (95% CI: 3 - 87); n/N = 1/61	(1 RCT) ²	⊕⊕○○ LOW ^{a,b,e,g}

1. Barret T, Bowden DJ, Greenberg DC, Brown CH, Wishart PD. Radiological staging in breast cancer: which asymptomatic patients to image and how. Br J Cancer; 2009.
 2. Kasem AR, Desai A, Daniell S, Sinha P.. Bone scan and liver ultrasound scan in the preoperative staging for primary breast cancer.. Breast J. ; 2006.
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	<p>represented; this suggest that only a subpopulation of these cases entered in the study and that they could be those with higher suspicious of having distal metastases.</p> <p>c. The proportion of patients actually staging investigated with more than one imaging tests was variable which could underestimated the exams' performance. All studies reported to include follow-up of patients although with different time frame.</p> <p>d. Some or most of the studies recruited consecutive patients from medical records (or prospectively) which could or could not have symptoms suggestive of metastases.</p> <p>e. The assessment of each individual tests is based in the number of patients that were examined who are a subpopulation of all those subject at this stage which could overestimate its performance measurements.</p> <p>f. Judgement about inconsistency was considered serious given that the reported detected rate was inconsistent with other studies performed in the same stage and applying similar procedures to identify distant metastases.</p> <p>g. Judgement of imprecision was considered serious as one or both of the confidence interval limits reached detection rates threshold which could potentially change the decision about requesting staging tests.</p>	
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS
<div>○ Large</div> <div>○ Moderate</div> <div>● Small</div> <div>○ Trivial</div> <div>○ Varies</div> <div>○ Don't know</div>	Outcomes	Impact	Nº of participants (studies)	Certainty of the evidence (GRADE)	The GDG judged by consensus that the undesirable effects were small.
	Detection rate: Combined tests (prevalence)	Pooled detection rate: 8 per 1,000 examinations (95% CI: 0 - 30); n/N = 15/1,958	(5 RCTs) ^{1,2,3,4,5}	⊕⊕○○ LOW ^{a,b,c,d}	
	Detection rate: Bone Scan	Pooled detection rate: 5 per 1,000 examinations (95% CI 0 - 21) n/N = 17/2,397	(5 RCTs) ^{1,2,4,6,7}	⊕⊕○○ LOW ^{a,b,d,e}	
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	0 - 2); n/N = 0/1,049		LOW ^{a,b,d,e}
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- a. Different reference standards were used, some included another imaging test without histological confirmation which is likely to incorrectly classify the condition
- b. Some studies included retrospective case records where inclusion criteria cannot be properly assessed, in some cases the distribution of stages at diagnosis is not that expected in the population, in particular stage I and stage II are under-represented; this suggest that only a subpopulation of these cases entered in the study and that they could be those with higher suspicious of having distal metastases.
- c. The proportion of patients actually staging investigated with more than one imaging tests was variable which could underestimated the exams' performance. All studies reported to include follow-up of patients although with different time frame.
- d. Some or most of the studies recruited consecutive patients from medical records (or prospectively) which could or could not have symptoms suggestive of metastases.
- e. The assessment of each individual tests is based in the number of patients that were examined who are a subpopulation of all those subject at this stage which could overestimate its performance measurements.
- f. Judgement of imprecision was considered serious as one or both of the confidence interval limits reached detection rates threshold which could potentially change the decision about requesting staging tests.

Outcomes	Impact	Nº of participants (studies)	Certainty of the evidence (GRADE)
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False positive: CT Pelvic - not reported		-	-
False positive: TC abdominal - not reported		-	-
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 - d. Some or most of the studies recruited consecutive patients from medical records (or prospectively) which could or could not have symptoms suggestive of metastases.

	<p>e. The assessment of each individual tests is based in the number of patients that were examined who are a subpopulation of all those subject at this stage which could overestimate its performance measurements.</p> <p>f. Judgement about inconsistency was considered serious given that the reported detected rate was inconsistent with other studies performed in the same stage and applying similar procedures to identify distant metastases.</p> <p>g. Judgement of imprecision was considered serious as one or both of the confidence interval limits reached detection rates threshold which could potentially change the decision about requesting staging tests.</p>	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ● Low ○ Moderate ○ High ○ No included studies 		The GDG judged by consensus that the certainty of the evidence was low.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes 		The GDG judged by consensus that there was possibly important uncertainty or variability in how much women value the main outcomes.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know 		<p>The GDG notes the low certainty of the evidence, notably for the detection rate with conventional staging exams.</p> <p>The GDG also notes the very high 5-year survival for patients with stage I breast cancer.</p> <p>As agreement could not be reached by consensus, voting was conducted among members without COL:</p> <p>*15 members voted for 'favours the comparison',</p> <p>*7 members voted for 'probably favors the intervention'.</p>

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS															
<ul style="list-style-type: none">● Large costs○ Moderate costs○ Negligible costs and savings○ Moderate savings○ Large savings○ Varies○ Don't know	<p>Direct evidence: Mean cost and utilization</p> <p>One Italian study (DePlacido 2017) determined the relative costs of staging and follow-up tests in a population of breast cancer patients in a Southern Italian region. The number and type of tests per patient were recorded 3 months before and 12 months after the date diagnosis of nonmetastatic breast cancer from 2001 to 2010.</p> <table><tr><th rowspan="2">Type of tests</th><th colspan="3">Estimated annual variation (2001-2010)</th></tr><tr><th>Mean cost¹ of imaging tests per patient (Euros)</th><th>Imaging utilization, % (95% CI)</th><th>Imaging-related costs, % (95% CI)</th></tr><tr><td>Chest radiograph, abdominal ultrasound, bone scan, and mammograms</td><td>Remain constant at 250 €</td><td>Increase 0.1% (-0.1–0.3)</td><td>Decrease 0.1% (-0.9 to 0.6)</td></tr><tr><td>CT, PET, and MRI</td><td>Increased from 350 € in 2001 to 800 € in 2010</td><td>Increase 15.7% (14.2–17.2)</td><td>Increase 19.4% (15.9–23.0)</td></tr></table> <p>¹Prices were reported in 2011 Euros value.</p>	Type of tests	Estimated annual variation (2001-2010)			Mean cost ¹ of imaging tests per patient (Euros)	Imaging utilization, % (95% CI)	Imaging-related costs, % (95% CI)	Chest radiograph, abdominal ultrasound, bone scan, and mammograms	Remain constant at 250 €	Increase 0.1% (-0.1–0.3)	Decrease 0.1% (-0.9 to 0.6)	CT, PET, and MRI	Increased from 350 € in 2001 to 800 € in 2010	Increase 15.7% (14.2–17.2)	Increase 19.4% (15.9–23.0)	<p>Indirect evidence:</p> <p>One study from Canada and two studies from the USA reported costs of imaging tests. The Canadian study reported that patients with stage II incurred higher imaging costs than those with stage I: CAD 535 per capita compared with CAD 204 per capita (2015 Canadian dollars) (Thavorn2016). The USA studies reported that the unitary cost per chest x-rays was USD 96.9, abdominal ultrasound USD 285, CT chest with contrast USD 239 to USD 510, CT abdominal-pelvis with contrast USD 305 to USD 696, body bone scan USD 658 to USD 853.8 (2013-2014 US dollars) (Louie2015, Pellet2016).</p> <p>The GDG notes that due to the lower detection rate for stage I breast cancer the costs per patient with metastasis detected are assumed to be</p>
Type of tests	Estimated annual variation (2001-2010)																
	Mean cost ¹ of imaging tests per patient (Euros)	Imaging utilization, % (95% CI)	Imaging-related costs, % (95% CI)														
Chest radiograph, abdominal ultrasound, bone scan, and mammograms	Remain constant at 250 €	Increase 0.1% (-0.1–0.3)	Decrease 0.1% (-0.9 to 0.6)														
CT, PET, and MRI	Increased from 350 € in 2001 to 800 € in 2010	Increase 15.7% (14.2–17.2)	Increase 19.4% (15.9–23.0)														

		greater than USD 100,000 per case detected. The GDG agreed by consensus that the costs are large.
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ● Low ○ Moderate ○ High ○ No included studies 	Low certainty of the evidence due to indirectness, and imprecision. Costs reported in the study may not be representative of other European settings since it was performed only in Campania, Italy. Also, there is imprecision in the results since the cost of each test was not reported. In fact, only the mean cost of imaging tests per patient (including chest radiograph, abdominal ultrasound, bone scan, and mammograms) were reported.	<p>The cost requirement evidence was based on a single study. The detection rate that was used in the cost study was 3/1000 for the AJCC 6th edition and 12/1000 according to the AJCC 5th edition.</p> <p>The GDG judged that the certainty of evidence of required resources was low.</p>

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies 	No relevant economic evaluations were identified	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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<ul style="list-style-type: none"> ○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know 		<p>The GDG notes that when the burden of tests is increased for patients with staging exams, there may be increased costs to patients depending on health care coverage of diagnostic tests for patients.</p> <p>If the wait time is long for publicly-funded imaging in a particular setting, patients may opt to pay out of pocket for accelerated staging exams, therefore reducing health equity. The GDG judged by consensus that the impact on health equity would vary.</p>
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Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know 		<p>The GDG notes that the population of stage I patients is much larger, and therefore the costs will be much larger, policy makers will therefore not likely find the intervention acceptable.</p> <p>The GDG considered that some women may strongly desire staging exams, while other women may be distressed by the staging exams.</p> <p>The GDG judged by consensus that the acceptability varied among women and other key stakeholders.</p>

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know 		<p>The GDG was not aware of any settings where staging exams using imaging for clinical stage I is routinely performed in current practice.</p> <p>As consensus was not reached, voting was conducted among GDG members without COI:</p>

		<p>*11 members voted 'probably no' 6 'varies'</p> <p>*1 member voted 'probably yes'.</p> <p>*One member did not register a vote.</p>
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SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			No known undesirable outcomes
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

The ECIBC's Guidelines Development Group suggests against using a staging exams with imaging in women with clinical stage I breast cancer (conditional recommendation, low certainty of the evidence).

Justification

Overall justification

As consensus was not reached, voting was conducted among members without COI: 15 members voted in favour of 'strong recommendation against the intervention', 7 members voted in favour of 'conditional recommendation against the intervention'. To make a strong recommendation, the GDG voting rules require a 80% majority in support. Therefore, a conditional recommendation against the intervention was made.

Detailed justification

Desirable Effects

The desirable effects of the intervention were judged to be trivial. The pooled combined detection rate of metastases (from 6 RCTs) was 6.33 and the 95% confidence interval was 0-24.8 per 1000 women with clinical stage I breast cancer that undergo conventional staging exams.

Undesirable Effects

The undesirable effects of the intervention were judged to be small. The pooled false positive rate was 32.4 per 1000 women with clinical stage I breast cancer who undergo staging exams.

Balance of effects

The balance of effects was judged to favour the comparison.

Resources required

The resources required for the intervention were judged to be large costs. The costs of conventional staging exams for women with stage I cancer was assumed to be greater than \$100,000 per metastasis detected, inferring from evidence on staging exams for women with clinical stage II cancer.

Subgroup considerations

The GDG noted that women with clinical stage I breast cancer receiving neo-adjuvant chemotherapy may be considered for conventional staging exams using imaging.

Implementation considerations

1. The GDG considered the definition of stage groups according to the American Joint Commission on Cancer TNM Anatomic Stage Groups (8th ed.) listed in the ECIBC glossary.
2. The GDG notes that there is still uncertainty with the evidence of detection rate using conventional staging exams with imaging.
3. The GDG notes that psychological support may be indicated to assist with follow-up of clinical stage I breast cancers in place of staging exams using imaging for reassurance of women who are very distressed about the potential for metastases.

Monitoring and evaluation

1. The GDG suggests monitoring and evaluation efforts to improve compliance with this suggestion to not conduct staging exams using imaging for clinical stage I breast cancers.
2. The GDG suggests assessment by the QASDG for recommendations and implementation of monitoring and evaluation.

Research priorities

1. The GDG suggests further research to provide higher quality evidence on the detection rate with staging exams using imaging in clinical stage I breast cancers.
2. The GDG suggests further research on clinical stage I breast cancers that are diagnosed and ultimately metastasise to determine causes, and whether the use of staging exams will impact outcomes.
3. The GDG suggests further research to assess the impact of staging exams using imaging for clinical stage I breast cancers with different higher risk histology groups.
4. The GDG suggests further research to assess possible subgroups within clinical stage I breast cancers and varying need for staging exams using imaging.
5. The GDG suggests research on non-ionizing and low-radiation dose alternatives for staging exams using imaging.