



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 III breast cancer without symptoms suggestive of metastases?	
POPULATION:	patients with clinical stage III 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: CT Chest; False positive: CT Chest; Detection rate: CT pelvic; False positive: CT pelvic; Detection rate: CT abdominal; False positive: CT abdominal ; Detection rate: XR Chest; False positive: XR Chest; 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. However, the risk for metastases is lower in early detected (clinical stage I and II) breast cancer than in later stages (clinical stage III). When prevalence of metastases is higher, the ratio between benefits and harms is expected to improve. Although, the staging interventions have the advantage of ensuring adequate treatment adapted to the tumour stage, it is also associated with some disadvantages like limited specificity, leading to psychological stress of the women, radiation (depending on the used technique) and high costs.
CONFLICT OF INTEREST:	Col's 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.

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
<div>○ Trivial</div> <div>○ Small</div> <div>○ Moderate</div> <div>● Large</div> <div>○ Varies</div> <div>○ Don't know</div>	Outcomes	Impact	No of participants (studies)	Certainty of the evidence (GRADE)	<p>In one study including 411 clinical stage II breast cancer patients (Bychkovsky 2016) 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 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).</p> <p>The GDG agreed by consensus that the desirable effects were large.</p>
	Detection rate: Combined tests (prevalence)	Pooled detection rate: 142 per 1,000 examinations (95%CI 113 - 175); n/N = 74/510	(5 RCTs) ^{1,2,3,4,5}	⊕⊕⊕○ MODERATE ^{a,b,c,d}	
	Detection rate: Bone Scan	Pooled detection rate: 103 per 1,000 examinations (95%CI: 53 - 167); n/N = 103/1,172	(4 RCTs) ^{2,3,6,7}	⊕○○○ VERY LOW ^{a,d,e,f}	
	Detection rate: CT Chest	Pooled detection rate: 60 per 1,000 examinations (95%CI: 39 - 87); n/N = 25/417	(1 RCT) ⁸	⊕⊕⊕○ MODERATE ^{a,e}	
	Detection rate: CT pelvic - not reported		-	-	

Detection rate: CT abdominal - not reported		-	-a
Detection rate: XR Chest	Pooled detection rate: 63 per 1,000 examinations (95% CI 16 - 131); n/N = 12/190	(3 RCTs) ^{2,3,9}	⊕○○○ VERY LOW ^{a,d,e,f}
Detection rate: US	Pooled detection rate: 57 per 1,000 examinations (95% CI: 12 - 157); n/N = 3/53	(1 RCT) ²	⊕⊕○○ LOW ^{a,e,f}

1. Hulikal N, Gajjala SR, Kalawat TC, Kottu R, Amancharla Yadagiri L.. Utility of [18F] Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (FDG PET/CT) in the Initial Staging and Response Assessment of Locally Advanced Breast Cancer Patients Receiving Neoadjuvant Chemotherapy.. Indian J Surg Oncol. ; 2015.
 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. Dillman RO, Chico S.. Radiologic tests after a new diagnosis of breast cancer.. Eff Clin Pract.; 2000.
 4. Ravaioli A, Tassinari D, Pasini G, Polselli 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.
 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. Koizumi M, Yoshimoto M, Kasumi F, Ogata E.. What do breast cancer patients benefit from staging bone scintigraphy?. Jpn J Clin Oncol.; 2001.
 7. 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.
 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.
 9. Louie RJ, Tonneson JE, Gowarty M, Goodney PP, Barth RJ Jr, Rosenkranz KM.. Complete blood counts, liver function tests, and chest x-rays as routine screening in early-stage breast cancer: value added or just cost?. Breast Cancer Res Treat.; 2015.
- a. Different reference standards were used, some included another imaging test without histological confirmation which is likely to incorrectly classify the condition.
 - b. 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.
 - c. Imaging for searching distant metastases is routine practice, therefore the risk of selected patient population undergoing staging is low also for retrospective studies.
 - 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.
 - 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 rate: 56 per 1,000 examinations (95%CI 33 - 84); n/N = 24/327	(2 RCTs) ^{1,2}	⊕⊕⊕○ MODERATE ^{a,b,c,d}
False positive: Bone Scan - not reported		-	- ^a
False positive: CT Chest	False positive: 141 per 1,000 examinations (95%CI 109 - 179); n/N = 59/417	(1 RCT) ³	⊕⊕⊕○ MODERATE ^{a,e}
False positive: CT pelvic - not reported		-	-
False positive: CT abdominal - not reported		-	-
False positive: XR Chest	False positive: 60 per 1,000 examinations (95%CI 20 - 133); n/N = 5/84	(1 RCT) ⁴	⊕○○○ VERY LOW ^{a,d,e,f}
False positive: US - not reported		-	-

1. Ravaioli A, Tassinari D, Pasini G, Polselli 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.
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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.

	<p>b. 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>c. Imaging for searching distant metastases is routine practice, therefore the risk of selected patient population undergoing staging is low also for retrospective studies.</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.</p> <p>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.</p>	
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Large ○ Moderate ○ Small ○ Trivial ○ Varies ○ Don't know 	Outcomes	Impact	Nº of participants (studies)	Certainty of the evidence (GRADE)	<p>Sensitivity analysis without Puglisi (2005):</p> <p>*Pooled false positive rate: 163.2 per 1000 examinations (95%CI 46.9 - 321.4); n/N = 46/309.</p> <p>The GDG agreed by consensus that the undesirable effects would be large.</p>
	Detection rate: Combined tests (prevalence)	Pooled detection rate: 142 per 1,000 examinations (95%CI 113 - 175); n/N = 74/510	(5 RCTs) ^{1,2,3,4,5}	⊕⊕⊕○ MODERATE ^{a,b,c,d}	
	Detection rate: Bone Scan	Pooled detection rate: 103 per 1,000 examinations (95%CI: 53 - 167); n/N = 103/1,172	(4 RCTs) ^{2,3,6,7}	⊕○○○ VERY LOW ^{a,d,e,f}	
	Detection rate: CT Chest	Pooled detection rate: 60 per 1,000 examinations (95%CI: 39 - 87); n/N = 25/417	(1 RCT) ⁸	⊕⊕⊕○ MODERATE ^{a,e}	
	Detection rate: CT pelvic - not reported		-	-	
	Detection rate: CT abdominal - not reported		-	- ^a	
	Detection rate: XR Chest	Pooled detection rate: 63 per 1,000 examinations (95% CI 16 - 131); n/N = 12/190	(3 RCTs) ^{2,3,9}	⊕○○○ VERY LOW ^{a,d,e,f}	

Detection rate: US	Pooled detection rate: 57 per 1,000 examinations (95% CI: 12 - 157); n/N = 3/53	(1 RCT) ²	 LOW ^{a,e,f}
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Outcomes	Impact	No of participants (studies)	Certainty of the evidence (GRADE)

False positive: Combined tests (prevalence)	Pooled false positive rate: 56 per 1,000 examinations (95%CI 33 - 84); n/N = 24/327	(2 RCTs) ^{1,2}	⊕⊕⊕○ MODERATE ^{a,b,c,d}
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False positive: CT pelvic - not reported		-	-
False positive: CT abdominal - not reported		-	-
False positive: XR Chest	False positive: 60 per 1,000 examinations (95%CI 20 - 133); n/N = 5/84	(1 RCT) ⁴	⊕○○○ VERY LOW ^{a,d,e,f}
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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.
 - e. The assessment of each individual tests is based in the number of patients that were examined who are

	f. a subpopulation of all those subject at this stage which could overestimate its performance. 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.	
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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 agreed by consensus that the certainty of the evidence of effects was moderate.

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 		<p>No systematic review for values and preferences regarding diagnostic exams was conducted.</p> <p>The GDG judged by consensus that there was possibly important uncertainty or variability.</p>

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>Voting was conducted because agreement was not reached consensus.</p> <p>*19 members voted in favour of 'favours the intervention'</p> <p>*2 members voted for 'probably favours the intervention',</p> <p>*2 members abstained and,</p> <p>*2 member was absent for the voting.</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: 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 costs were lower than the cost for stage 2 staging exams using imaging.</p> <p>The GDG also notes that the number of patients presenting in this group (stage III) constitutes a smaller population.</p> <p>The GDG agreed by consensus that the resources required were moderate.</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)														
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	<p>Direct evidence: Unitary cost and cost of detecting metastatic disease</p> <p>One UK study (Barret 2009) estimated the health-care costs of detecting metastases by stage of disease and mode of imaging staging in a population of 3,398 newly diagnosed breast cancer patients during 1999 to 2007. The estimation was based on local costing taking into consideration staffing, consumable and hardware expenses. Calculations were carried out based on the observed true-positive rates and the added expense generated by false-positive imaging results.</p> <table> <tr> <th rowspan="2">Type of tests</th><th rowspan="2">Unitary cost¹ (British Pounds)</th><th>Cost¹ of detecting 1 patient with metastatic disease by breast cancer stage</th></tr> <tr> <th>III</th></tr> <tr> <td>Chest radiograph</td><td>80 £</td><td rowspan="3">4,021 £</td></tr> <tr> <td>Ultrasound liver</td><td>176 £</td></tr> <tr> <td>Bone scan</td><td>184 £</td></tr> <tr> <td>CT (chest, abdomen, and pelvis)</td><td>271 £</td><td>2,405 £</td></tr> </table> <p>¹Value prices were not clearly reported (data was collected from 1999 to 2007).</p>	Type of tests	Unitary cost ¹ (British Pounds)	Cost ¹ of detecting 1 patient with metastatic disease by breast cancer stage	III	Chest radiograph	80 £	4,021 £	Ultrasound liver	176 £	Bone scan	184 £	CT (chest, abdomen, and pelvis)	271 £	2,405 £	
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Chest radiograph	80 £	4,021 £														
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Bone scan	184 £															
CT (chest, abdomen, and pelvis)	271 £	2,405 £														

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 	<p>Low certainty of the evidence due to indirectness, and imprecision. Costs reported in the studies may not be representative of other European settings since they were performed only in Campania, Italy or in the UK. For the UK study, in addition, value prices were not reported (data was collected from 1999 to 2007) and may not represent current costs. Also, there is imprecision in the results since the cost of each test was not reported.</p>	<p>The cost requirement evidence was based only on two studies with serious concerns regarding the indirectness and imprecision. 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
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<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.	
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know 		<p>The GDG notes that due to a smaller population size there is a lower impact on equity.</p> <p>The GDG agreed by consensus that there would be probably no impact on health equity.</p>

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 agreed by consensus that it would probably be acceptable.</p>

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ● Probably yes 		<p>The GDG agreed by consensus that it would probably be feasible.</p>

<input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		
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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 recommends using conventional staging exams with imaging in women with clinical stage III breast cancer (strong recommendation, moderate certainty of the evidence).

Justification

Overall justification

Voting was conducted as agreement was not reached by consensus: 20 members (91%) for 'strong recommendation for the intervention', 2 members (9%) voted for 'conditional recommendation for the intervention'.

Detailed justification

Desirable Effects

The GDG judged that the desirable effects were large with a pooled detection rate for combined tests of 142 per 1,000 examinations for women with stage III breast cancer.

Undesirable Effects

The GDG judged that the false positives contribute to large undesirable anticipated effects, however, notes that false positives are of lower concern for women with stage III breast cancer.

Certainty of evidence

The GDG judged that the certainty of the evidence of effects was moderate.

Balance of effects

The GDG judged that the balance of effects favours the intervention.

Resources required

The GDG judged that there would be moderate resources required for this intervention.

Subgroup considerations

The GDG also notes that age and presence of comorbidities of the patient may be a consideration in the decision of whether to conduct staging exams with imaging as this may change the choice of treatment.

Implementation considerations

None considered.

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.

Monitoring and evaluation

The GDG suggests monitoring that women with **clinical** stage III breast cancer receive staging exams using imaging.

Research priorities

1. The GDG suggests research assessing the cause of false positive cases to minimize the number of false positives and the undue stress that this poses on patients with **clinical** stage III breast cancer.
2. The GDG suggests research on non-ionizing and low-radiation dose alternatives for staging exams using imaging.