



**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 18F-FDG PET-CT staging exams vs. no PET staging exams be used for patients with clinical stage I breast cancer without symptoms suggestive of metastases?**

<b>POPULATION:</b>	patients with clinical stage I breast cancer without symptoms suggestive of metastases
<b>INTERVENTION:</b>	18F-FDG PET-CT staging exams
<b>COMPARISON:</b>	no PET staging exams
<b>MAIN OUTCOMES:</b>	Detection rate; False positive;
<b>SETTING:</b>	European Union
<b>PERSPECTIVE:</b>	Population (National Health System)
<b>BACKGROUND:</b>	<p>The main cause of death from breast cancer is 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 clinical stages (stage 3). 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.</p>
<b>CONFLICT OF INTEREST:</b>	<p>ColIs 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 Col 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>

## ASSESSMENT

### Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ No</li> <li>○ Probably no</li> <li>○ Probably yes</li> <li>● Yes</li> <li>○ Varies</li> <li>○ Don't know</li> </ul>	<p>The main cause of death from breast cancer is 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 clinical stages (stage 3). 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.</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>One study did not identify distant metastases among 23 women with triple negative breast cancer (TNBC) at stage I (1) One study did not reveal significant difference in the rate of distant metastases at clinical stages I to III between breast cancer patients less than 40 years versus those ≥40 years (<i>p value</i>=1.0). One study in 254 patients with BC clinical stage II and III evaluated by 18FDG-PET-CT (2), 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 total number of patients included in the stage I were unexpectedly small compared to the known distribution of breast cancer patients per stage. Given this limited number of participants and that studies were of observational design, we considered that there is a risk that these cases represent a very selected population and might have a higher rate of distant metastases.</p> <p>The clinical impact of detecting distant metastasis (in practice moving the patient to Stage IV) can be considered on two domains:</p>
	Detection rate	Pooled detection rate: 16 per 1000 examinations (95% CI: 0 - 59); n/N = 3/80	(6 RCTs) <sup>1,2,3,4,5,6</sup>	⊕⊕○○ LOW <sup>a,b,c,d</sup>	
<div><div>1. Ulaner, G. A., Castillo, R., Goldman, D. A., Wills, J., Riedl, C. C., Pinker-Domenig, K., Jochelson, M. S., Gonen, M.. (18)F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. Eur J Nucl Med Mol Imaging; Oct 2016.</div><div>2. Sen, F., Akpinar, A. T., Ogur, U., Duman, G., Tamgac, F., Alper, E.. The impact of PET/CT imaging performed in the early postoperative period on the management of breast cancer patients. Nucl Med Commun; Jun 2013.</div><div>3. Riedl, C. C., Slobod, E., Jochelson, M., Morrow, M., Goldman, D. A., Gonen, M., Weber, W. A., Ulaner, G. A.. Retrospective analysis of 18F-FDG PET/CT for staging asymptomatic breast cancer patients younger than 40 years. J Nucl Med; Oct 2014.</div><div>4. Lebon, V., Alberini, J. L., Pierga, J. Y., Dieras, V., Jehanno, N., Wartski, M.. Rate of Distant Metastases on 18F-FDG PET/CT at Initial Staging of Breast Cancer: Comparison of Women Younger and Older Than 40 Years. J Nucl Med; Feb 2017.</div><div>5. Hogan, M. P., Goldman, D. A., Dashevsky, B., Riedl, C. C., Gonen, M., Osborne, J. R., Jochelson, M., Hudis, C., Morrow, M., Ulaner, G. A.. Comparison of 18F-FDG PET/CT for Systemic Staging of Newly Diagnosed Invasive Lobular Carcinoma Versus Invasive Ductal Carcinoma. J Nucl Med; Nov 2015.</div></div>					

6. Ulaner, G. A., Castillo, R., Goldman, D. A. 18F-FDG-PET/CT for systemic staging of patients with newly diagnosed ER-positive and HER2-positive breast cancer. Eur J Nucl Med Mol ; 2017.
- a. Judgement of imprecision depends on the panel decision about the detection rate threshold which leads to change decision.
- b. Overall, included studies had small sample sizes, therefore confidence interval are widen.
- c. Different reference standards were used across studies some included another imaging test without histological confirmation which is likely to incorrectly classify the condition. Additional follow up were not implemented in all cases.
- d. Some studies collected its data from medical registries on retrospective designs which preclude them from implementing standard procedures and quality of data.

Outcomes	Impact	Nº of participants (studies)	Certainty of the evidence (GRADE)
False positive	Pooled detection rate: 0.0 per 1000 examinations (95% CI: 0 - 36); n/N = 0/51	(3 RCTs) <sup>1,2,3</sup>	⊕⊕○○ LOW <sup>a,b,c,d</sup>

1. Ulaner, G. A., Castillo, R., Goldman, D. A., Wills, J., Riedl, C. C., Pinker-Domenig, K., Jochelson, M. S., Gonen, M.. (18)F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. Eur J Nucl Med Mol Imaging; Oct 2016.
2. Riedl, C. C., Slobod, E., Jochelson, M., Morrow, M., Goldman, D. A., Gonen, M., Weber, W. A., Ulaner, G. A.. Retrospective analysis of 18F-FDG PET/CT for staging asymptomatic breast cancer patients younger than 40 years. J Nucl Med; Oct 2014.
3. Hogan, M. P., Goldman, D. A., Dashevsky, B., Riedl, C. C., Gonen, M., Osborne, J. R., Jochelson, M., Hudis, C., Morrow, M., Ulaner, G. A.. Comparison of 18F-FDG PET/CT for Systemic Staging of Newly Diagnosed Invasive Lobular Carcinoma Versus Invasive Ductal Carcinoma. J Nucl Med; Nov 2015.
- a. Judgement of imprecision depends on the panel decision about the detection rate threshold which leads to change decision.
- b. Overall, included studies had small sample sizes, therefore confidence interval are widen.
- c. Different reference standards were used across studies some included another imaging test without histological confirmation which is likely to incorrectly classify the condition. Additional follow up were not implemented in all cases.
- d. Some studies collected its data from medical registries on retrospective designs which preclude them from implementing standard procedures and quality of data.

### Survival

The 5-year relative survival rate for women with breast cancer by stage is approximately:

-Stage 0 or stage I breast cancer is close to 100%. -- Metastatic, or stage IV breast cancers survival rate of about 22%.

### Quality of life

This domain is influenced by the change of treatment plans in each clinical stage according to the presence of distant metastases

-Stage I and II not needing adjuvant chemotherapy (HER2 positive or triple negative breast cancer < 5 mm): potentially minor change or no change. Radiotherapy might or might not be indicated to primary lesion and in single cases of oligometastases.

-Stage I and II that need adjuvant chemotherapy (HER2 positive or triple negative and tumor size ≥ 5 mm): potentially meaningful change depending on: 1) ER/PR positive/HER2 negative breast cancer: endocrine treatment only, no chemotherapy 2) HER positive: less intense chemotherapy regime; 3) triple negative: only mono-chemotherapy instead of poly-chemotherapy. Radiotherapy might or might not be indicated to primary lesion and in single cases of oligometastases. On those HER2+ possibly addition of Pertuzumab to the anti-HER2 therapy.

### **Glycolytic activity with 18F-FDG PET/CT, tumor biology, and prognosis ((3) Systematic Review)**

*"Maximum standardized uptake value (SUVmax) increases with the biological aggressiveness of the tumors; high-grade, hormone receptor-negative, have higher SUVmax. However, a reproducible SUVmax cutoff that would predict tumor biology has yet to be established"*

*"The prognostic impact of the SUVmax of the primary tumor is controversial. Whereas some authors found no association between tumor 18F-FDG uptake and prognosis, others reported that patients with high tumor uptake had*

		worse outcomes. Furthermore, a single and reproducible SUVmax has yet to be established"								
Undesirable Effects										
How substantial are the undesirable anticipated effects?										
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS								
<div><div>○ Large</div><div>○ Moderate</div><div>● Small</div><div>○ Trivial</div><div>○ Varies</div><div>○ Don't know</div></div>	<table><tr><th>Outcomes</th><th>Impact</th><th>No of participants (studies)</th><th>Certainty of the evidence (GRADE)</th></tr><tr><td>Detection rate</td><td>Pooled detection rate: 16 per 1000 examinations (95% CI: 0 - 59); n/N = 3/80</td><td>(6 RCTs)<sup>1,2,3,4,5,6</sup></td><td>⊕⊕○○ LOW<sup>a,b,c,d</sup></td></tr></table> <div><div><div>1. Ulaner, G. A., Castillo, R., Goldman, D. A., Wills, J., Riedl, C. C., Pinker-Domenig, K., Jochelson, M. S., Gonen, M.. (18)F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. Eur J Nucl Med Mol Imaging; Oct 2016.</div><div>2. Sen, F., Akpınar, A. T., Ogur, U., Duman, G., Tamgac, F., Alper, E.. The impact of PET/CT imaging performed in the early postoperative period on the management of breast cancer patients. Nucl Med Commun; Jun 2013.</div><div>3. Riedl, C. C., Slobod, E., Jochelson, M., Morrow, M., Goldman, D. A., Gonen, M., Weber, W. A., Ulaner, G. A.. Retrospective analysis of 18F-FDG PET/CT for staging asymptomatic breast cancer patients younger than 40 years. J Nucl Med; Oct 2014.</div><div>4. Lebon, V., Alberini, J. L., Pierga, J. Y., Dieras, V., Jehanno, N., Wartski, M.. Rate of Distant Metastases on 18F-FDG PET/CT at Initial Staging of Breast Cancer: Comparison of Women Younger and Older Than 40 Years. J Nucl Med; Feb 2017.</div><div>5. Hogan, M. P., Goldman, D. A., Dashevsky, B., Riedl, C. C., Gonen, M., Osborne, J. R., Jochelson, M., Hudis, C., Morrow, M., Ulaner, G. A.. Comparison of 18F-FDG PET/CT for Systemic Staging of Newly Diagnosed Invasive Lobular Carcinoma Versus Invasive Ductal Carcinoma. J Nucl Med; Nov 2015.</div><div>6. Ulaner, G. A.,Castillo,R.,Goldman,D. A. 18F-FDG-PET/CT for systemic staging of patients with newly diagnosed ER-positive and HER2-positive breast cancer. Eur J Nucl Med Mol ; 2017.</div></div><div><div><div>a. Judgement of imprecision depends on the panel decision about the detection rate threshold which leads to change decision.</div><div>b. Overall, included studies had small sample sizes, therefore confidence interval are widen.</div><div>c. Different reference standards were used across studies some included another imaging test without histological confirmation which is likely to incorrectly classify the condition. Additional follow up were not implemented in all cases.</div><div>d. Some studies collected its data from medical registries on retrospective designs which preclude them from implementing standard procedures and quality of data.</div></div></div></div>	Outcomes	Impact	No of participants (studies)	Certainty of the evidence (GRADE)	Detection rate	Pooled detection rate: 16 per 1000 examinations (95% CI: 0 - 59); n/N = 3/80	(6 RCTs) <sup>1,2,3,4,5,6</sup>	⊕⊕○○ LOW <sup>a,b,c,d</sup>	Two studies reported false positives rates for patients in clinical stage II and III as overall, from 7.6 (Groheux 2012) to 11.8 (Groheux 2011) per 1000 examined women.
Outcomes	Impact	No of participants (studies)	Certainty of the evidence (GRADE)							
Detection rate	Pooled detection rate: 16 per 1000 examinations (95% CI: 0 - 59); n/N = 3/80	(6 RCTs) <sup>1,2,3,4,5,6</sup>	⊕⊕○○ LOW <sup>a,b,c,d</sup>							

Outcomes		Impact	No of participants (studies)	Certainty of the evidence (GRADE)
False positive		Pooled detection rate: 0.0 per 1000 examinations (95% CI: 0 - 36); n/N = 0/51	(3 RCTs) <sup>1,2,3</sup>	⊕⊕○○ LOW <sup>a,b,c,d</sup>
<ol style="list-style-type: none"> <li>1. Ulaner, G. A., Castillo, R., Goldman, D. A., Wills, J., Riedl, C. C., Pinker-Domenig, K., Jochelson, M. S., Gonen, M.. (18)F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. Eur J Nucl Med Mol Imaging; Oct 2016.</li> <li>2. Riedl, C. C., Slobod, E., Jochelson, M., Morrow, M., Goldman, D. A., Gonen, M., Weber, W. A., Ulaner, G. A.. Retrospective analysis of 18F-FDG PET/CT for staging asymptomatic breast cancer patients younger than 40 years. J Nucl Med; Oct 2014.</li> <li>3. Hogan, M. P., Goldman, D. A., Dashevsky, B., Riedl, C. C., Gonen, M., Osborne, J. R., Jochelson, M., Hudis, C., Morrow, M., Ulaner, G. A.. Comparison of 18F-FDG PET/CT for Systemic Staging of Newly Diagnosed Invasive Lobular Carcinoma Versus Invasive Ductal Carcinoma. J Nucl Med; Nov 2015.</li> </ol> <ol style="list-style-type: none"> <li>a. Judgement of imprecision depends on the panel decision about the detection rate threshold which leads to change decision.</li> <li>b. Overall, included studies had small sample sizes, therefore confidence interval are widen.</li> <li>c. Different reference standards were used across studies some included another imaging test without histological confirmation which is likely to incorrectly classify the condition. Additional follow up were not implemented in all cases.</li> <li>d. Some studies collected its data from medical registries on retrospective designs which preclude them from implementing standard procedures and quality of data.</li> </ol>				
Certainty of evidence				
What is the overall certainty of the evidence of effects?				
JUDGEMENT	RESEARCH EVIDENCE			ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>● Very low</li> <li>○ Low</li> <li>○ Moderate</li> <li>○ High</li> <li>○ No included studies</li> </ul>				The GDG agreed by consensus that the certainty of evidence is very 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"><li>○ Important uncertainty or variability</li><li>● Possibly important uncertainty or variability</li><li>○ Probably no important uncertainty or variability</li><li>○ No important uncertainty or variability</li><li>○ No known undesirable outcomes</li></ul>		<p>The GDG noted that the results of PET-CT may dictate whether a change in the treatment is warranted.</p> <p>The GDG agreed by consensus that there is possibly important uncertainty or variability in the values.</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"><li>● Favors the comparison</li><li>○ Probably favors the comparison</li><li>○ Does not favor either the intervention or the comparison</li><li>○ Probably favors the intervention</li><li>○ Favors the intervention</li><li>○ Varies</li><li>○ Don't know</li></ul>		<p>The GDG agreed by consensus that the balance between the desirable and undesirable effects favours the comparison.</p>

## Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS																														
<ul style="list-style-type: none"><li>● Large costs</li><li>○ Moderate costs</li><li>○ Negligible costs and savings</li><li>○ Moderate savings</li><li>○ Large savings</li><li>○ Varies</li><li>○ Don't know</li></ul>	<p>One study performed in the Netherlands (4) reported the costs associated with implementing PET and PET/CT with FES or FDG as an upfront imaging test for diagnosing metastatic breast cancer in oestrogen receptor-positive women with symptoms. The reported unitary costs were:</p> <p>CT: EUR 199</p> <p>FES-PET: EUR 1 505</p> <p>FDG-PET: EUR 1 505</p> <p>The unit prices of the tests based on tariffs of The Dutch Healthcare Authority.</p> <p><b>Costs informed by the GDG</b></p> <p><b>Cost PET-CT</b></p> <table><tr><th>Test</th><th>Country, year value</th><th>Setting</th><th>Cost</th></tr><tr><td>PET-CT staging*</td><td>Germany, 2017</td><td>Hospital</td><td>1987,76 Euro</td></tr><tr><td>PET alone</td><td>Germany, 2017</td><td>Hospital</td><td>1337,04 Euro</td></tr><tr><td>PET alone</td><td>Italy, 2012-2016</td><td>Hospital</td><td>1286,00 Euro</td></tr></table> <p>* including all the cost for machine, radionuclide and the work of doctors and technicians</p> <p><b>Resources required PET-CT</b></p> <table><tr><th>Resources</th><th>Cost</th></tr><tr><td>PET-CT machine</td><td>2.5 million Euro</td></tr><tr><td>Reactor to make the radionuclide</td><td>NA</td></tr><tr><td>Nuclear medicine doctor</td><td>NA</td></tr><tr><td>Radiologist</td><td>NA</td></tr><tr><td>Nurse/technician running the machine</td><td>NA</td></tr><tr><td>Medical physicist</td><td>NA</td></tr></table>	Test	Country, year value	Setting	Cost	PET-CT staging*	Germany, 2017	Hospital	1987,76 Euro	PET alone	Germany, 2017	Hospital	1337,04 Euro	PET alone	Italy, 2012-2016	Hospital	1286,00 Euro	Resources	Cost	PET-CT machine	2.5 million Euro	Reactor to make the radionuclide	NA	Nuclear medicine doctor	NA	Radiologist	NA	Nurse/technician running the machine	NA	Medical physicist	NA	<p>The cost per patient with stage I breast cancer receiving PET-CT is about EUR 1500, so the GDG agreed by consensus that the resource requirements are large.</p>
Test	Country, year value	Setting	Cost																													
PET-CT staging*	Germany, 2017	Hospital	1987,76 Euro																													
PET alone	Germany, 2017	Hospital	1337,04 Euro																													
PET alone	Italy, 2012-2016	Hospital	1286,00 Euro																													
Resources	Cost																															
PET-CT machine	2.5 million Euro																															
Reactor to make the radionuclide	NA																															
Nuclear medicine doctor	NA																															
Radiologist	NA																															
Nurse/technician running the machine	NA																															
Medical physicist	NA																															



## 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"> <li>○ Very low</li> <li>○ Low</li> <li>○ Moderate</li> <li>● High</li> <li>○ No included studies</li> </ul>	Have direct information from hospitals in Europe.	The GDG agreed the certainty of the evidence that resource requirements are large is high.

## 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"> <li>○ Favors the comparison</li> <li>○ Probably favors the comparison</li> <li>○ Does not favor either the intervention or the comparison</li> <li>○ Probably favors the intervention</li> <li>○ Favors the intervention</li> <li>○ Varies</li> <li>● No included studies</li> </ul>	No economic evaluations were identified	No studies were included.

## Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ Reduced</li> <li>● Probably reduced</li> <li>○ Probably no impact</li> <li>○ Probably increased</li> <li>○ Increased</li> <li>○ Varies</li> <li>○ Don't know</li> </ul>	No systematic review was carried out.	The GDG agreed that equity would probably be reduced. In many countries there may be problems providing PET-CT to these patients.

## Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><li>● No</li><li>○ Probably no</li><li>○ Probably yes</li><li>○ Yes</li><li>○ Varies</li><li>○ Don't know</li></ul>	No systematic review was carried out.	The GDG agreed by consensus that this intervention would not be acceptable to key stakeholders due to large costs.

## Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><li>● No</li><li>○ Probably no</li><li>○ Probably yes</li><li>○ Yes</li><li>○ Varies</li><li>○ Don't know</li></ul>	No systematic review was carried out.	The GDG agreed by consensus that this intervention would not be feasible to implement.

## 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 ○
---	--	---	--	---

## CONCLUSIONS

### Recommendation

For patients with clinical stage I breast cancer without symptoms suggestive of metastases , the ECIBC's Guidelines Development Group (GDG) recommends against using positron emission tomography-computed tomography (PET-CT) staging exams (strong recommendation, very low certainty of the evidence).

### Justification

#### Overall Justification

The GDG agreed by consensus to recommend strongly against this intervention.

### Subgroup considerations

For triple negative tumours and HER2 positive evidence suggests that there is no additional benefit because of no increased risks from metastases.

### Implementation considerations

None were considered by the GDG.

### Monitoring and evaluation

None were considered by the GDG.

### Research priorities

The GDG suggests research to clarify the clinical significance of true positives (for all stages).

## REFERENCES SUMMARY

1. Ulaner, G. A., Castillo, R., Goldman, D. A., Wills, J., Riedl, C. C., Pinker-Domenig, K., Jochelson, M. S., Gonen, M.. (18)F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. Eur J Nucl Med Mol Imaging; Oct 2016.
2. Groheux D, Hindié E, Delord M, Giacchetti S, Hamy AS, de Bazelaire C, de Roquancourt A, Vercellino L, Toubert ME, Merlet P, Espié M.. Prognostic impact of (18)FDG-PET-CT findings in clinical stage III and IIB breast cancer. J Natl Cancer Inst; 2012.
3. Caresia Aroztegui AP, García Vicente AM, Alvarez Ruiz S, Delgado Bolton RC, Orcajo Rincon J, Garcia Garzon JR, et al.. 18F-FDG PET/CT in breast cancer: Evidence-based recommendations in initial staging.. Tumour Biol.; 2017.
4. Koleva-Kolarova RG, Greuter MJ, van Kruchten M, Vermeulen KM, Feenstra T, Buskens E, et al.. The value of PET/CT with FES or FDG tracers in metastatic breast cancer: a computer simulation study in ER-positive patients.. Br J Cancer.; 2015.