



**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	
<b>Should screening using digital breast tomosynthesis in addition to digital mammography vs. digital mammography alone be used in organised screening programmes for early detection of breast cancer in asymptomatic women?</b>	
<b>POPULATION:</b>	Asymptomatic women attending an organised breast cancer screening programme
<b>INTERVENTION:</b>	screening using digital breast tomosynthesis (including synthesised 2D images) in addition to digital mammography
<b>COMPARISON:</b>	digital mammography
<b>MAIN OUTCOMES:</b>	Breast cancer mortality, breast cancer stage, breast cancer detection, interval breast cancer, recall for assessment, quality of life, other-cause mortality, adverse effects (including radiation exposure, radiation induced cancers-related to radiation dose, overdiagnosis, false positive related adverse effects
<b>SETTING:</b>	European Union
<b>PERSPECTIVE:</b>	Population (National Health System)
<b>BACKGROUND:</b>	<p>Breast cancer is the second most common cancer in the world and, by far, the most frequent cancer among women, with an estimated 2 088 849 new cancer cases diagnosed in 2018 (11.6% of all cancers) (Ferlay, 2018). Breast cancer ranks as the fourth cause of death from cancer overall (626 679 deaths) (Ferlay, 2018).</p> <p>Screening programmes play a crucial role in early breast cancer detection; it can increase the chance of survival as well as have an impact on breast cancer mortality. Digital mammography (DM) remains the best method to detect breast cancer in an early stage. DM is a technique of imaging which produces a 2D image of the 3D organ. Inevitably, this implies that lesions can be obscured by superposition of dense tissue. Indeed, the superposition of tissue can lead to false positives as well as false negatives.</p> <p>Breast cancer is the second most common cancer in the world and, by far, the most frequent cancer among women, with an estimated 2 088 849 new cancer cases diagnosed in 2018 (11.6% of all cancers) (Ferlay, 2018). Breast cancer ranks as the fourth cause of death from cancer overall (626 679 deaths) (Ferlay, 2018).</p> <p>Screening programmes play a crucial role in early breast cancer detection; it can increase the chance of survival as well as have an impact on breast cancer mortality. Digital mammography (DM) remains the best method to detect breast cancer in an early stage. DM is a technique of imaging which produces a 2D image of the 3D organ. Inevitably, this implies that lesions can be obscured by superposition of dense tissue. Indeed, the superposition of tissue can lead to false positives as well as false negatives.</p> <p>Digital breast tomosynthesis (DBT) is an imaging technique based on a series of low dose images of the breast taken from different angles and one compression, and has the potential to partly overcome tissue superposition thus improving detection of breast lesions through minimization of masking effects in DM (Rafferty EA, 2013, Gur D, 2009). The series of projections is then processed by a reconstruction algorithm to estimate the 3D appearance of the breast which can be viewed in successive slices. In screening</p>

	<p>trials, tomosynthesis has been used in addition to a 2D image done with 2D DM, regardless whether synthetic 2D images of the DBT series were available or not.</p> <p><b>This recommendation was updated in January 2020. Previous versions of the recommendation are available on the ECIBC website.</b></p>
<b>CONFLICT OF INTEREST:</b>	<p>Management of Conflicts of Interest (Col): Cols for all Guidelines Development Group (GDG) members were assessed and managed by the Joint Research Centre (JRC) following an established procedure in line with European Commission 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: Jan Danes, Solveig Hofvind, Elsa Pérez, and Kenneth Young. Miranda Langendam was not allowed to vote due to the established rules for external experts.</p> <p>For more information please visit <a href="https://healthcare-quality.jrc.ec.europa.eu/discover-ecibc/governance/ecibc-working-groups">https://healthcare-quality.jrc.ec.europa.eu/discover-ecibc/governance/ecibc-working-groups</a></p>

## ASSESSMENT

<b>Problem</b> 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>Breast cancer is the second most common cancer in the world and, by far, the most frequent cancer among women, with an estimated 2 088 849 new cancer cases diagnosed in 2018 (11.6% of all cancers), it ranks as the fourth cause of death from cancer overall (626,679 deaths) (Ferlay, 2018).</p> <p>DM is widely used in screening and diagnosis of breast cancer. However, some aspects such as superposition of breast tissue limits the sensitivity and specificity of mammography and false-positives and false negatives are an issue (JRC Technical Report PICO 1-3, contract FWC443094012015; available upon request). DBT might provide better imaging and discriminative capacity in these cases.</p>	<p><b>Updated on January 2020</b></p> <p>There was discussion about whether or not this question is still a priority. The panel remarked that there are ongoing or recent studies and some regulators are still considering the intervention in question.</p>
<b>Desirable Effects</b> How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ Trivial</li> <li>○ Small</li> <li>● Moderate</li> <li>○ Large</li> <li>○ Varies</li> <li>○ Don't know</li> </ul>	<p><b>Date of last search: January 2020</b></p>	<p>The GDG agreed that the desirable outcomes are: breast cancer detection, false positive recall for assessment (reduction). Recall for assessment was not considered as a critical outcome because it is already included in the outcome "false positive recall for assessment".</p> <p>During the updating of the searches, in January 2020, 4 new paired studies meeting the inclusion</p>

Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with digital mammography	Risk difference with (Post-meeting_rev PRU) Should screening using digital breast tomosynthesis in addition to digital mammography
Breast cancer detection <sup>a</sup>	1727333 (24 observational studies) <sup>1,10,11,12,13,14,15,16,17,18,19,2,20,21,22,23,24,3,4,5,6,7,8,9,b,c</sup>	⊕⊕⊕○ MODERATE <sup>d</sup>	RR 1.26 (1.20 to 1.31) <sup>e</sup>	Study population  439 per 100,000 <sup>c</sup>	  <b>114 more per 100,000</b> (88 more to 136 more)
False positive recall for assessment <sup>f</sup>	1718301 (24 observational studies) <sup>1,10,11,12,13,15,16,17,18,19,2,20,21,22,23,24,3,4,5,6,7,8,9,b</sup>	⊕⊕○○ LOW <sup>d,g</sup>	RR 0.81 (0.77 to 0.85)	Study population  9,566 per 100,000	  <b>1,817 fewer per 100,000</b> (2,200 fewer to 1,435 fewer)
Breast cancer stage (inferred from invasive cancer detection rate)	1075535 (15 observational studies) <sup>12,13,14,15,18,19,2,20,23,24,25,3,5,7,9,b,c</sup>	⊕⊕○○ LOW <sup>d,g,h</sup>	RR 1.34 (1.26 to 1.44)	Study population  311 per 100,000 <sup>c</sup>	  <b>106 more per 100,000</b> (81 more to 137 more)
Invasive cancers/total cancers	5297 (15 observational studies) <sup>12,13,14,15,18,19,2,20,23,24,25,3,5,7,9</sup>	⊕⊕○○ LOW <sup>d,g,h</sup>	RR 1.03 (0.97 to 1.09)	Study population  71 per 100	  <b>2 more per 100</b> (2 fewer to 6 more)

criteria for desirable effects were identified and added to the SoF: 1 RCT (Pattacini P et al., 2018), and 3 observational studies (Skaane P, 2018, Houssami N, 2018, Romero Martín S, 2018).

During the update of January 2020, the panel decided to include unpaired studies for all outcomes. The included studies, both paired (i.e. comparison made within participants, all participants underwent 2D mammography and DBT) and unpaired designs (i.e. comparison of separate groups that underwent DBT additional to 2D mammography versus 2D mammography), reported data for all outcomes. Results from both types of design were consistent across outcomes, and data was therefore pooled.

The new studies provided additional information on false positive recall for assessment and radiation exposure. Critical outcomes such as breast cancer mortality, quality of life, or other-causes of mortality are still not measured in the included studies.




The currently included studies only present data from first round DBT in addition to DM screening.

We included only studies that reported both breast cancer detection rate and false positive recall for assessment. If needed we calculated the former using other available data (e.g. recall rate or specificity).

Grade/tumour characteristics/prognostics might clarify the amount of possible overdiagnosis in this population. A systematic review of these characteristics was not pre-planned and results of such search and analysis are not available.

From the total breast cancers detected, a proportion will be a desirable health outcome and another proportion of the increased detection will be overdiagnosis. However, the panel suggested that detection rate is a desirable effect. Overdiagnosis which is part of this number is considered an undesirable effect. The proportion of this is not known conclusively.

The inconsistency of the results of interval cancer

	Interval breast cancer <sup>i</sup>	784166 (8 observational studies) <sup>16,19,26,27,28,29,30,31,b,j,k</sup>	 LOW <sup>d,l</sup>	RR 1.04 (0.90 to 1.20)	Study population		(not fitting with the expected direction of the results) suggests that a large proportion of detected cancers may be indeed overdiagnosis. Some members of the panel questioned if the observation of increased interval cancers are indeed creating an inconsistency because of the biology being possibly different.  Due to the similar data and the similar assumptions about the evidence available, the GDG decided to make the same judgement for desirable effects as for the recommendation on DBT vs DM (for additional information refer to the specific recommendation published). For that judgement, consensus was not reached and voting was conducted among the GDG members, the majority voted “moderate”, but there was considerable disagreement (1 member voted “small”, <b>7 members voted “moderate”</b> , 2 members voted “large”, 6 members voted “don’t know” and 1 abstained).
					103 per 100,000	<b>4 more per 100,000</b> (10 fewer to 21 more)	
	Radiation exposure	0 (1 RCT) <sup>20</sup>	 HIGH <sup>m</sup>	-	The median dose per examination was 6.40 mGy (IQR, 5.68–7.36 mGy) and 4.84 mGy (IQR, 4.24–5.72 mGy) for DBT and DM, respectively, meaning that the dose for DBT in addition to DM was 11.24 mGy (2.3 times higher than DM alone).		
	Radiation exposure	0 (3 observational studies) <sup>32,33,34</sup>	 VERY LOW <sup>m,n</sup>	-	Radiation doses for digital mammography plus tomosynthesis were approximately twice that reported for digital mammography alone. <sup>o</sup>		
	Breast cancer mortality - not reported	-	-	-	-	-	
	Quality of life - not reported	-	-	-	-	-	
	Radiation induced cancers-related to radiation dose - not reported	-	-	-	-	-	
	Overdiagnosis - not reported - not reported	-	-	-	-	-	
	Other causes of mortality - not reported	-	-	-	-	-	

1. Romero Martín S, Raya Povedano JL, Cara García M, Santos Romero AL, Pedrosa Garriguet M, Álvarez Benito M.. Prospective study aiming to compare 2D mammography and tomosynthesis + synthesized mammography in terms of cancer detection and recall.. Eur Radiol; 2018.
2. Bernardi D, Macaskill P, Pellegrini M, Valentini M, Fantò C, Ostilio L, Tuttobene P, Luparia A, Houssami N.. Breast cancer screening with tomosynthesis (3D mammography) with acquired or synthetic 2D mammography compared with 2D mammography alone (STORM-2): a population-based prospective study.. Lancet Oncol; 2016.
3. Ciatto S, Houssami N, Bernardi D, Caumo F, Pellegrini M, Brunelli S, et al. Integration of 3D digital mammography with tomosynthesis for population breast-cancer screening (STORM): a prospective comparison study. The Lancet Oncology; 2013.
4. Johnson K, Zackrisson, Rosso, Sartor, Saal, Anderson, Lang. Tumor Characteristics and Molecular Subtypes in Breast Cancer Screening with Digital Breast Tomosynthesis: The Malmö Breast Tomosynthesis Screening Trial. Radiology; 2019.
5. Skaane P, Bandos, Niklason, Sebuødegård, Østerås, Gullien, Gur, Hofvind. Digital Mammography versus Digital Mammography Plus Tomosynthesis in Breast Cancer Screening: The Oslo Tomosynthesis Screening Trial. Radiology; 2019.
6. Lång K, Nergården M, Andersson I, Rosso A, Zackrisson S. False positives in breast cancer screening with one-view breast tomosynthesis: An analysis of findings leading to recall, work-up and biopsy rates in the Malmö Breast Tomosynthesis Screening Trial. Eur Radiol; 2016.
7. Powell, J. L., Hawley, J. R., Lipari, A. M., Yildiz, V. O., Erdal, B. S., Carkaci, S.. Impact of the Addition of Digital Breast Tomosynthesis (DBT) to Standard 2D Digital Screening Mammography on the Rates of Patient Recall, Cancer Detection, and Recommendations for Short-term Follow-up. Acad Radiol; 2016.
8. Miglioretti, D. L., Abraham, L., Lee, C. I., Buist, D. S. M., Herschorn, S. D., Sprague, B. L., Henderson, L. M., Tosteson, A. N. A., Kerlikowske, K.. Digital Breast Tomosynthesis: Radiologist Learning Curve. Radiology; 2019.
9. McCarthy, A. M., Kontos, D., Synnestvedt, M., Tan, K. S., Heitjan, D. F., Schnall, M., Conant, E. F.. Screening outcomes following implementation of digital breast tomosynthesis in a general-population screening program. J Natl Cancer Inst; 2014.
10. Lourenco, A. P., Barry-Brooks, M., Baird, G. L., Tuttle, A., Mainiero, M. B.. Changes in recall type and patient treatment following implementation of screening digital breast tomosynthesis. Radiology; 2014.
11. Haas, B. M., Kalra, V., Geisel, J., Raghu, M., Durand, M., Philpotts, L. E.. Comparison of tomosynthesis plus digital mammography and digital mammography alone for breast cancer screening. Radiology; 2013.
12. Greenberg, J. S., Javitt, M. C., Katzen, J., Michael, S., Holland, A. E.. Clinical performance metrics of 3D digital breast tomosynthesis compared with 2D digital mammography for breast cancer screening in community practice. AJR Am J Roentgenol; 2014.
13. Friedewald, S. M., Rafferty, E. A., Rose, S. L., Durand, M. A., Plecha, D. M., Greenberg, J. S., Hayes, M. K., Copit, D. S., Carlson, K. L., Cink, T. M., Barke, L. D., Greer, L. N., Miller, D. P., Conant, E. F.. Breast cancer screening using tomosynthesis in combination with digital mammography. Jama; 2014.
14. Freer, P. E., Riegert, J., Eisenmenger, L., Ose, D., Winkler, N., Stein, M. A., Stoddard, G. J., Hess, R.. Clinical implementation of synthesized mammography with digital breast tomosynthesis in a routine clinical practice. Breast Cancer Res Treat; 2017.
15. Durand, M. A., Haas, B. M., Yao, X., Geisel, J. L., Raghu, M., Hooley, R. J., Horvath, L. J., Philpotts, L. E.. Early clinical experience with digital breast tomosynthesis for screening mammography. Radiology; 2014.
16. Conant, E. F., Barlow, W. E., Herschorn, S. D., Weaver, D. L., Beaber, E. F., Tosteson, A. N. A., Haas, J. S., Lowry, K. P., Stout, N. K., Trentham-Dietz, A., diFlorio-Alexander, R. M., Li, C. I.,

- Schnall, M. D., Onega, T., Sprague, B. L.. Association of Digital Breast Tomosynthesis vs Digital Mammography With Cancer Detection and Recall Rates by Age and Breast Density. JAMA Oncol; 2019.
17. Bahl, M., Pinnamaneni, N., Mercaldo, S., McCarthy, A. M., Lehman, C. D.. Digital 2D versus Tomosynthesis Screening Mammography among Women Aged 65 and Older in the United States. Radiology; 2019.
  18. Auiero, M. P., Gavenonis, S. C., Benjamin, R., Zhang, Z., Holt, J. S.. Clinical Performance of Synthesized Two-dimensional Mammography Combined with Tomosynthesis in a Large Screening Population. Radiology; 2017.
  19. Alsheik, N. H., Dabbous, F., Pohlman, S. K., Troeger, K. M., Gliklich, R. E., Donadio, G. M., Su, Z., Menon, V., Conant, E. F.. Comparison of Resource Utilization and Clinical Outcomes Following Screening with Digital Breast Tomosynthesis Versus Digital Mammography: Findings From a Learning Health System. Acad Radiol; 2018.
  20. Pattacini P, Nitrosi A, Giorgi Rossi P, Iotti V, Ginocchi V, Ravaioli S, Vacondio R, Braglia L, Cavuto S, Campari C, Group., RETomo, Working. Digital Mammography versus Digital Mammography Plus Tomosynthesis for Breast Cancer Screening: The Reggio Emilia Tomosynthesis Randomized Trial.. Radiology ; 2018.
  21. Destounis, S., Arieno, A., Morgan, R.. Initial Experience with Combination Digital Breast Tomosynthesis Plus Full Field Digital Mammography or Full Field Digital Mammography Alone in the Screening Environment. Journal of Clinical Imaging Science; 2014.
  22. Giess, C.S., et al.. Comparing Diagnostic Performance of Digital Breast Tomosynthesis and Full-Field Digital Mammography in a Hybrid Screening Environment. Roentgenol; 2017.
  23. Starikov, A., et al.. 2D mammography, digital breast tomosynthesis, and ultrasound: Which should be used for the different breast densities in breast cancer screening?. Clinical Imaging; 2016.
  24. Sharpe, R.E. Jr et al.. Increased Cancer Detection Rate and Variations in the Recall Rate Resulting from implementation of 3D Digital Breast Tomosynthesis into a Population-base Screening program. Radiology; 2016.
  25. Rose, S. L., Tidwell, A. L., Ice, M. F., Nordmann, A. S., Sexton, R., Jr., Song, R.. A reader study comparing prospective tomosynthesis interpretations with retrospective readings of the corresponding FFDM examinations. Acad Radiol; 2014.
  26. Houssami N, Bernardi D, Caumo F, Brunelli S, Fantò C, Valentini M, et al. Interval breast cancers in the screening with tomosynthesis or standard mammography (STORM) population-based trial. Breast; 2018.
  27. Skaane P, Sebuødegård S, Bandos AI, Gur D, Østerås BH, Gullien R, Hofvind S.. Performance of breast cancer screening using digital breast tomosynthesis: results from the prospective population-based Oslo Tomosynthesis Screening Trial. Breast Cancer Res Treat; 2018.
  28. Bahl M, Gaffney S, McCarthy AM, Lowry KP, Dang PA, Lehman CD. Breast Cancer Characteristics Associated with 2D Digital Mammography versus Digital Breast Tomosynthesis for Screening-detected and Interval Cancers. Radiology; 2018.
  29. Bernardi, D., Gentilini, M. A., De Nisi, M., Pellegrini, M., Fanto, C., Valentini, M., Sabatino, V., Luparia, A., Houssami, N.. Effect of implementing digital breast tomosynthesis (DBT) instead of mammography on population screening outcomes including interval cancer rates: Results of the Trento DBT pilot evaluation. Breast; 2019.
  30. Hovda, T., Holen, A. S., Lang, K., Albertsen, J. L., Bjørndal, H., Brandal, S. H. B., Sahlberg, K. K., Skaane, P., Suhrke, P., Hofvind, S.. Interval and Consecutive Round Breast Cancer after Digital Breast Tomosynthesis and Synthetic 2D Mammography versus Standard 2D Digital Mammography in BreastScreen Norway. Radiology; 2019.
  31. McDonald, E. S., Oustimov, A., Weinstein, S. P., Synnestvedt, M. B., Schnall, M., Conant, E. F.. Effectiveness of Digital Breast Tomosynthesis Compared With Digital Mammography: Outcomes Analysis From 3 Years of Breast Cancer Screening. JAMA Oncol; 2016.
  32. Paulis LE, Lobbes MB, Lalji UC, Gelissen N, Bouwman RW, Wildberger JE, et al. Radiation exposure of





	<p>digital breast tomosynthesis using an antiscatter grid compared with full-field digital mammography. Invest Radiol; 2015.</p> <p>33. Wallis MG, Moa E,Zanca F,Leifland K,Danielsson M. Two-view and single-view tomosynthesis vs. full-field digital mammography: high-resolution X-ray imaging observer study. Radiology; 2012.</p> <p>34. Skaane P, Bandos AI,Gullien R,Eben EB,Ekseth U,Haakenaasen U,et al.. Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program.. Radiology.; 2013.</p> <ul style="list-style-type: none"> <li>a. Calculated as the total number of women with positive screening/overall number of screening examinations</li> <li>b. Cohort studies provided partial diagnostic information. The risk of bias was assessed using an ad-hoc modified QUADAS-2 tool.</li> <li>c. Median or mean of the control group of the included studies as appropriate unless otherwise specified.</li> <li>d. Concerns for risk of bias due to reference standard was not blinded to the index tests. Additionally, there was variability in the number of readings, readers' experience and number of readers (i.e. single or double) across studies.</li> <li>e. Relative effect was adjusted for paired design.</li> <li>f. Calculated as the number of false positives/overall number of screening examinations - total number of cancers</li> <li>g. Despite only women with suggestive findings of malignancy being followed-up, the panel agreed that there was not an important risk of information bias, as the same strategy was implemented in both arms of the included studies, and the effects were consistent across them.</li> <li>h. Invasive cancer stage is a surrogate outcome of cumulative incidence of advance breast cancer.</li> <li>i. Calculates as the number of women with breast cancer after a negative screening/ overall number of screening examinations</li> <li>j. Data from one round (most recent 2008-2009) included in control arm (DM) (Skane 2018)</li> <li>k. Houssami 2018 gives data from women who did not participate in OTST study (external cohort) included as control arm (DM)</li> <li>l. Wide 95%CI and low number of events</li> <li>m. Results were consistent independently of the technology used (Hologic Selenia Dimension or Senographe Dimension).</li> <li>n. Radiation exposure is a surrogate outcome of "other cancer related to radiation".</li> <li>o. Doses are known to vary (diagnostic reference levels are typically country/region and technology specific).</li> </ul>	
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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>	Date of last search: January 2020					<p>The GDG agreed that the undesirable outcomes are: interval breast cancer, overdiagnosis, and radiation exposure.</p> <p>Interval cancer data are consistent with the comparison of DBT vs DM in the same population.</p> <p>As for desirable effects the GDG considered that the data and the assumptions about the evidence available are similar to the one used for the recommendation on DBT vs DM (for additional information refer to the specific recommendation published). The GDG decided to judge the undesirable effects as “moderate” due to the additional radiation dose caused by the use of both technologies.</p>	
	Outcomes	Nº of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		
					Risk with digital mammography		Risk difference with (Post-meeting_rev PRU) Should screening using digital breast tomosynthesis in addition to digital mammography
	Breast cancer detection <sup>a</sup>	1727333 (24 observational studies) <sup>1,10,11,12,13,14,15,16,17,18,19,2,20,21,22,23,24,3,4,5,6,7,8,9,b,c</sup>	⊕⊕⊕○ MODERATE <sup>d</sup>	RR 1.26 (1.20 to 1.31) <sup>e</sup>	Study population		
					439 per 100,000 <sup>c</sup>		114 more per 100,000 (88 more to 136 more)
	False positive recall for assessment <sup>f</sup>	1718301 (24 observational studies) <sup>1,10,11,12,13,15,16,17,18,19,2,20,21,22,23,24,3,4,5,6,7,8,9,b</sup>	⊕⊕○○ LOW <sup>d,g</sup>	RR 0.81 (0.77 to 0.85)	Study population		
					9,566 per 100,000		1,817 fewer per 100,000 (2,200 fewer to 1,435 fewer)
	Breast cancer stage (inferred from invasive cancer detection rate)	1075535 (15 observational studies) <sup>12,13,14,15,18,19,2,20,23,24,25,3,5,7,9,b,c</sup>	⊕⊕○○ LOW <sup>d,g,h</sup>	RR 1.34 (1.26 to 1.44)	Study population		
					311 per 100,000 <sup>c</sup>		106 more per 100,000 (81 more to 137 more)

	Invasive cancers/total cancers	5297 (15 observational studies) <sup>12,13,14,15,18,19,2,20,23,24,25,3,5,7,9</sup>	 LOW <sup>d,g,h</sup>	RR 1.03 (0.97 to 1.09)	Study population	
					71 per 100	<b>2 more per 100</b> (2 fewer to 6 more)
	Interval breast cancer <sup>i</sup>	784166 (8 observational studies) <sup>16,19,26,27,28,29,30,31,b,j,k</sup>	 LOW <sup>d,j</sup>	RR 1.04 (0.90 to 1.20)	Study population	
					103 per 100,000	<b>4 more per 100,000</b> (10 fewer to 21 more)
	Radiation exposure	0 (1 RCT) <sup>20</sup>	 HIGH <sup>m</sup>	-	The median dose per examination was 6.40 mGy (IQR, 5.68–7.36 mGy) and 4.84 mGy (IQR, 4.24–5.72 mGy) for DBT and DM, respectively, meaning that the dose for DBT in addition to DM was 11.24 mGy (2.3 times higher than DM alone).	
	Radiation exposure	0 (3 observational studies) <sup>32,33,34</sup>	 VERY LOW <sup>m,n</sup>	-	Radiation doses for digital mammography plus tomosynthesis were approximately twice that reported for digital mammography alone. <sup>o</sup>	
	Breast cancer mortality - not reported	-	-	-	-	-
	Quality of life - not reported	-	-	-	-	-
	Radiation induced cancers-related to radiation dose - not reported	-	-	-	-	-

Overdiagnosis - not reported - not reported	-	-	-	-	-
Other causes of mortality - not reported	-	-	-	-	-

1. Romero Martín S, Raya Povedano JL, Cara García M, Santos Romero AL, Pedrosa Garriguet M, Álvarez Benito M.. Prospective study aiming to compare 2D mammography and tomosynthesis + synthesized mammography in terms of cancer detection and recall.. Eur Radiol; 2018.
2. Bernardi D, Macaskill P, Pellegrini M, Valentini M, Fantò C, Ostilio L, Tuttobene P, Luparia A, Houssami N.. Breast cancer screening with tomosynthesis (3D mammography) with acquired orsynthetic 2D mammography compared with 2D mammography alone (STORM-2): a population-based prospective study.. Lancet Oncol; 2016.
3. Ciatto S, Houssami N, Bernardi D, Caumo F, Pellegrini M, Brunelli S, et al. Integration of 3D digital mammography with tomosynthesis for population breast-cancer screening (STORM): a prospective comparison study. The Lancet Oncology; 2013.
4. Johnson K, Zackrisson, Rosso, Sartor, Saal, Anderson, Lang. Tumor Characteristics and Molecular Subtypes in Breast Cancer Screening with Digital Breast Tomosynthesis: The Malmö Breast Tomosynthesis Screening Trial. Radiology; 2019.
5. Skaane P, Bandos, Niklason, Sebuødegård, Østerås, Gullien, Gur, Hofvind. Digital Mammography versus Digital Mammography Plus Tomosynthesis in Breast Cancer Screening: The Oslo Tomosynthesis Screening Trial. Radiology; 2019.
6. Lång K, Nergården M, Andersson I, Rosso A, Zackrisson S. False positives in breast cancer screening with one-view breast tomosynthesis: An analysis of findings leading to recall, work-up and biopsy rates in the Malmö Breast Tomosynthesis Screening Trial. Eur Radiol; 2016.
7. Powell, J. L., Hawley, J. R., Lipari, A. M., Yildiz, V. O., Erdal, B. S., Carkaci, S.. Impact of the Addition of Digital Breast Tomosynthesis (DBT) to Standard 2D Digital Screening Mammography on the Rates of Patient Recall, Cancer Detection, and Recommendations for Short-term Follow-up. Acad Radiol; 2016.
8. Miglioretti, D. L., Abraham, L., Lee, C. I., Buist, D. S. M., Herschorn, S. D., Sprague, B. L., Henderson, L. M., Tosteson, A. N. A., Kerlikowske, K.. Digital Breast Tomosynthesis: Radiologist Learning Curve. Radiology; 2019.
9. McCarthy, A. M., Kontos, D., Synnestvedt, M., Tan, K. S., Heitjan, D. F., Schnall, M., Conant, E. F.. Screening outcomes following implementation of digital breast tomosynthesis in a general-population screening program. J Natl Cancer Inst; 2014.
10. Lourenco, A. P., Barry-Brooks, M., Baird, G. L., Tuttle, A., Mainiero, M. B.. Changes in recall type and patient treatment following implementation of screening digital breast tomosynthesis. Radiology; 2014.
11. Haas, B. M., Kalra, V., Geisel, J., Raghu, M., Durand, M., Philpotts, L. E.. Comparison of tomosynthesis plus digital mammography and digital mammography alone for breast cancer screening. Radiology; 2013.
12. Greenberg, J. S., Javitt, M. C., Katzen, J., Michael, S., Holland, A. E.. Clinical performance metrics of 3D digital breast tomosynthesis compared with 2D digital mammography for breast cancer screening in community practice. AJR Am J Roentgenol; 2014.
13. Friedewald, S. M., Rafferty, E. A., Rose, S. L., Durand, M. A., Plecha, D. M., Greenberg, J. S., Hayes, M. K., Copit, D. S., Carlson, K. L., Cink, T. M., Barke, L. D., Greer, L. N., Miller, D. P.,

	<p>Conant, E. F.. Breast cancer screening using tomosynthesis in combination with digital mammography. <i>Jama</i>; 2014.</p> <p>14. Freer, P. E., Riegert, J., Eisenmenger, L., Ose, D., Winkler, N., Stein, M. A., Stoddard, G. J., Hess, R.. Clinical implementation of synthesized mammography with digital breast tomosynthesis in a routine clinical practice. <i>Breast Cancer Res Treat</i>; 2017.</p> <p>15. Durand, M. A., Haas, B. M., Yao, X., Geisel, J. L., Raghu, M., Hooley, R. J., Horvath, L. J., Philpotts, L. E.. Early clinical experience with digital breast tomosynthesis for screening mammography. <i>Radiology</i>; 2014.</p> <p>16. Conant, E. F., Barlow, W. E., Herschorn, S. D., Weaver, D. L., Beaber, E. F., Tosteson, A. N. A., Haas, J. S., Lowry, K. P., Stout, N. K., Trentham-Dietz, A., diFlorio-Alexander, R. M., Li, C. I., Schnall, M. D., Onega, T., Sprague, B. L.. Association of Digital Breast Tomosynthesis vs Digital Mammography With Cancer Detection and Recall Rates by Age and Breast Density. <i>JAMA Oncol</i>; 2019.</p> <p>17. Bahl, M., Pinnamaneni, N., Mercaldo, S., McCarthy, A. M., Lehman, C. D.. Digital 2D versus Tomosynthesis Screening Mammography among Women Aged 65 and Older in the United States. <i>Radiology</i>; 2019.</p> <p>18. Aujero, M. P., Gavenonis, S. C., Benjamin, R., Zhang, Z., Holt, J. S.. Clinical Performance of Synthesized Two-dimensional Mammography Combined with Tomosynthesis in a Large Screening Population. <i>Radiology</i>; 2017.</p> <p>19. Alsheik, N. H., Dabbous, F., Pohlman, S. K., Troeger, K. M., Gliklich, R. E., Donadio, G. M., Su, Z., Menon, V., Conant, E. F.. Comparison of Resource Utilization and Clinical Outcomes Following Screening with Digital Breast Tomosynthesis Versus Digital Mammography: Findings From a Learning Health System. <i>Acad Radiol</i>; 2018.</p> <p>20. Pattacini P, Nitrosi A, Giorgi Rossi P, Iotti V, Ginocchi V, Ravaioli S, Vacondio R, Braglia L, Cavuto S, Campari C, Group., RETomo, Working. Digital Mammography versus Digital Mammography Plus Tomosynthesis for Breast Cancer Screening: The Reggio Emilia Tomosynthesis Randomized Trial.. <i>Radiology</i> ; 2018.</p> <p>21. Destounis, S, Arieno, A, Morgan R.. Initial Experience with Combination Digital Breast Tomosynthesis Plus Full Field Digital Mammography or Full Field Digital Mammography Alone in the Screening Environment. <i>Journal of Clinical Imaging Science</i>; 2014.</p> <p>22. Giess, C.S., et al.. Comparing Diagnostic Performance of Digital Breast Tomosynthesis and Full-Field Digital Mammography in a Hybrid Screening Environment. <i>Roentgenol</i>; 2017.</p> <p>23. Starikov, A., et al.. 2D mammography, digital breast tomosynthesis, and ultrasound: Which should be used for the different breast densities in breast cancer screening?. <i>Clinical Imaging</i>; 2016.</p> <p>24. Sharpe, R.E. Jr et al.. Increased Cancer Detection Rate and Variations in the Recall Rate Resulting from implementation of 3D Digital Breast Tomosynthesis into a Population-base Screening program. <i>Radiology</i>; 2016.</p> <p>25. Rose, S. L., Tidwell, A. L., Ice, M. F., Nordmann, A. S., Sexton, R., Jr., Song, R.. A reader study comparing prospective tomosynthesis interpretations with retrospective readings of the corresponding FFDM examinations. <i>Acad Radiol</i>; 2014.</p> <p>26. Houssami N, Bernardi D, Caumo F, Brunelli S, Fantò C, Valentini M, et al. Interval breast cancers in the screening with tomosynthesis or standard mammography (STORM) population-based trial. <i>Breast</i>; 2018.</p> <p>27. Skaane P, Sebuødegård S, Bandos AI, Gur D, Østerås BH, Gullien R, Hofvind S.. Performance of breast cancer screening using digital breast tomosynthesis: results from the prospective population-based Oslo Tomosynthesis Screening Trial. <i>Breast Cancer Res Treat</i>; 2018.</p> <p>28. Bahl M, Gaffney S, McCarthy AM, Lowry KP, Dang PA, Lehman CD. Breast Cancer Characteristics Associated with 2D Digital Mammography versus Digital Breast Tomosynthesis for Screening-detected and Interval Cancers. <i>Radiology</i>; 2018.</p> <p>29. Bernardi, D., Gentilini, M. A., De Nisi, M., Pellegrini, M., Fanto, C., Valentini, M., Sabatino, V., Luparia, A., Houssami, N.. Effect of implementing digital breast tomosynthesis (DBT) instead of</p>	
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	<p>mammography on population screening outcomes including interval cancer rates: Results of the Trento DBT pilot evaluation. Breast; 2019.</p> <p>30. Hovda, T., Holen, A. S., Lang, K., Albertsen, J. L., Bjørndal, H., Brandal, S. H. B., Sahlberg, K. K., Skaane, P., Suhrke, P., Hofvind, S.. Interval and Consecutive Round Breast Cancer after Digital Breast Tomosynthesis and Synthetic 2D Mammography versus Standard 2D Digital Mammography in BreastScreen Norway. Radiology; 2019.</p> <p>31. McDonald, E. S., Oustimov, A., Weinstein, S. P., Synnestvedt, M. B., Schnall, M., Conant, E. F.. Effectiveness of Digital Breast Tomosynthesis Compared With Digital Mammography: Outcomes Analysis From 3 Years of Breast Cancer Screening. JAMA Oncol; 2016.</p> <p>32. Paulis LE, Lobb MB, Lalji UC, Gelissen N, Bouwman RW, Wildberger JE, et al. Radiation exposure of digital breast tomosynthesis using an antiscatter grid compared with full-field digital mammography. Invest Radiol; 2015.</p> <p>33. Wallis MG, Moa E, Zanca F, Leifland K, Danielsson M. Two-view and single-view tomosynthesis vs. full-field digital mammography: high-resolution X-ray imaging observer study. Radiology; 2012.</p> <p>34. Skaane P, Bandos AI, Gullien R, Eben EB, Ekseth U, Haakenaasen U, et al.. Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program.. Radiology.; 2013.</p> <p>a. Calculated as the total number of women with positive screening/overall number of screening examinations</p> <p>b. Cohort studies provided partial diagnostic information. The risk of bias was assessed using an ad-hoc modified QUADAS-2 tool.</p> <p>c. Median or mean of the control group of the included studies as appropriate unless otherwise specified.</p> <p>d. Concerns for risk of bias due to reference standard was not blinded to the index tests. Additionally, there was variability in the number of readings, readers' experience and number of readers (i.e. single or double) across studies.</p> <p>e. Relative effect was adjusted for paired design.</p> <p>f. Calculated as the number of false positives/overall number of screening examinations - total number of cancers</p> <p>g. Despite only women with suggestive findings of malignancy being followed-up, the panel agreed that there was not an important risk of information bias, as the same strategy was implemented in both arms of the included studies, and the effects were consistent across them.</p> <p>h. Invasive cancer stage is a surrogate outcome of cumulative incidence of advance breast cancer.</p> <p>i. Calculates as the number of women with breast cancer after a negative screening/ overall number of screening examinations</p> <p>j. Data from one round (most recent 2008-2009) included in control arm (DM) (Skane 2018)</p> <p>k. Houssami 2018 gives data from women who did not participate in OTST study (external cohort) included as control arm (DM)</p> <p>l. Wide 95%CI and low number of events</p> <p>m. Results were consistent independently of the technology used (Hologic Selenia Dimension or Senographe Dimension).</p> <p>n. Radiation exposure is a surrogate outcome of "other cancer related to radiation".</p> <p>o. Doses are known to vary (diagnostic reference levels are typically country/region and technology specific).</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"> <li>● Very low</li> <li>○ Low</li> <li>○ Moderate</li> <li>○ High</li> <li>○ No included studies</li> </ul>		Due to indirectness and inconsistency of the estimates for the critical outcomes prioritised by the GDG the certainty of the 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><b>Date of last search: April 2016</b></p> <p>No specific studies focusing in DBT were identified. The findings, all from mammography studies (JRC Technical Report PICO 10-11, contract FWC443094012015; available upon request), however, are likely to be generalisable to DBT, as both screening tests are associated with similar desirable and undesirable effects.</p> <p>A systematic review shows that participants in mammography screening programmes place a low value on the psychosocial and physical effects of false positive results and overdiagnosis (JRC Technical Report PICO 10-11, contract FWC443094012015). Women generally consider these undesirable effects acceptable (low certainty). However, these findings are of limited value, mainly given the significant concerns regarding the adequacy of the information provided to women, in order to make an informed decision about participation. Also, acceptability of false positive results is based on studies of participants who had already received a false positive result. Their preference may differ from the general population. Another finding is that breast cancer screening represents a significant burden for some women due to the associated psychological distress and inconvenience.</p> <p>Regarding breast cancer diagnosis, there is very limited data available on women' views. One of the main themes identified in the literature is that people disvalue highly the anxiety caused by delays in the receipt of results of diagnostic procedures, or by a lack of understanding of the tests due to suboptimal communication with physicians (moderate certainty). Also, people have a higher overall preference towards more comfortable, brief diagnostic procedures (moderate certainty).</p>	From the studies reviewed there was not much confidence in the findings and there is, therefore, uncertainty in how much people value the main outcomes. The GDG agreed that the increase in breast cancer detection, as well as the variation in recall rate, and the increase in radiation exposure are likely to be valued very differently by women.

## 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>As consensus was not reached, voting was conducted among the GDG members to judge balance between desirable and undesirable effects: 2 members voted “probably favours the comparison”, <b>13 members voted “does not favour either”</b>, 1 member voted “don’t know” and 1 abstained.</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><b>Date of last search: January 2020. No new evidence was included.</b></p> <p>Costs (2016 fees) used in the Medicaid model for 25,495 women aged 40 to 65 years in the US (Miller JD, 2017):</p> <p>1) <b>DM screening fee per patient</b> (including Computer-Assisted Diagnosis): <b>USD 95.18</b></p> <p>2) <b>DM in addition to DBT screening fee per patient</b> (including CAD): <b>USD 132.04</b></p>	<p><b>As no new evidence was included, the GDG members used the same judgement made in the previous version of this criterion, using previous considerations.</b></p> <p>A new study was identified reporting data about costs (Miller JD, 2017). The results from this study are reported under research evidence. The GDG agreed that resources required for moving from DM alone to DBT in addition to DM may include, amongst other factors: costs of the technology, capital costs of the machines and the lifetime of the machine, data transport and capacity for data storage, and additional time for radiologists to read DBT in addition to DM images, and increased time for the DBT in addition to DM compared to DM alone. Based on the information from three observational studies identified from the systematic review of Gilbert et al. (Gilbert FJ, 2016) radiologists’ reading time would have an increase of between 100% and 200% for DBT in addition to DM compared with DM alone (Bernardi D, 2012, Wallis MG, 2012, Skaane P, 2013). This corresponds to absolute times of 77-191 seconds for DBT in addition to DM and 33-67 seconds for DM alone.</p>

<b>Certainty of evidence of required resources</b> 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>	The certainty of the evidence is low due to indirectness. The study of Miller et al. (Miller JD, 2017) was performed in the US using data for women aged 40 to 65 years attending an annual DM screening.	
<b>Cost effectiveness</b> 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>	<b>Date of last search: January 2020. No new evidence was included.</b>	<p><b>As no new evidence was included, the GDG decided to consider the indirect evidence used for the recommendation on DBT vs DM (for additional information refer to the specific recommendation published) to inform this judgement.</b></p> <p>The GDG judge that the cost-effectiveness probably favours DM alone. This is even clearer than for the comparison DBT vs DM due to the need of conducting an additional DM, and the GDG assumption that the increase of sensitivity is due to the DBT alone and not the additional DM.</p>
<b>Equity</b> 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>	<b>Date of last search: April 2016</b>	The GDG felt that within screening programmes there may be policy decisions to restrict the programme if there are increased costs and the screening programme is unable to fund universal participation. This could have an influence on equity in either direction.



## 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>	<p><b>Date of last search: April 2016</b></p> <p>No specific studies focusing on DBT in addition to DM were identified. The findings, all from DM studies, however, are likely to be generalisable to DBT in addition to DM, as both (DBT and DM) are associated with similar desirable and undesirable effects.</p> <p>However, a systematic review (JRC Technical Report PICO 16-17, contract FWC443094032016; available upon request) found the following barriers associated with breast cancer screening with DM: (a) lack of knowledge and misperceptions regarding preventive medicine and breast health (high certainty of evidence), (b) poor communication skills of healthcare providers (high certainty of evidence), (c) poor accessibility to breast screening, especially among women with disabilities (high certainty of evidence), (d) fear and stress related to the procedure and the possibility of cancer diagnosis (high certainty of evidence), (e) pain and discomfort during the procedure (moderate certainty of evidence), (f) embarrassment and shyness during the procedure (moderate certainty of evidence), (g) lack of support and encouragement from family members, caregivers and social network (moderate certainty of evidence), (h) lack of information regarding the available resources (low certainty of evidence) and (i) low prioritisation of breast cancer screening (low certainty of evidence). Women and relevant stakeholders expressed similar opinions.</p>	<p><u>Participants:</u></p> <p>There is likely variability in acceptability for women. If there is a higher radiation dose, women may be more concerned. Additional compression time for the test and/or additional compressions might be necessary depending on the manufacturer of the device. Women who come for screening may be concerned that if they only have DM, and are not offered DBT, they are not getting the screening technology with the highest detection rate. Women may appreciate the increased confidence in the screening result if there is higher breast cancer detection when screening with DBT in addition to DM compared to screening with DM alone. Participation rates in the trials reviewed are high, which may indicate their general acceptability of screening with DBT in addition to DM compared to DM alone.</p> <p><u>Radiologists:</u></p> <p>DBT may be preferred by radiologists reading screening tests because their certainty in the diagnosis may be higher when using DBT in addition to DM compared to using DM alone.</p> <p><u>Policy makers:</u></p> <p>In settings with universal healthcare coverage, for directors of hospitals and screening programmes, carrying out DBT as well as DM may not be acceptable because there will likely be increased costs.</p>

## 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>	<p><b>Date of last search: April 2016</b></p>	<p>The GDG felt that in contexts where there are the resources to support this and where there is access to new technologies that are capable of DBT, it is feasible. For other countries without the technology and resources to support this it may not be feasible. In addition, although DBT requires some extra training for radiologists, this was not seen by GDG as a major barrier to implementation.</p> <p>The need to establish quality standards for synthesised 2D imaging for implementation was mentioned by the GDG.</p>

## SUMMARY OF JUDGEMENTS

CRITERIA	PREVIOUS VERSION JUNE 2018	UPDATE JANUARY 2020
PROBLEM	Yes	Yes
DESIRABLE EFFECTS	Don't know	Moderate
UNDESIRABLE EFFECTS	Varies	Moderate
CERTAINTY OF EVIDENCE	Very low	The same as original
VALUES	Important uncertainty or variability	The same as original
BALANCE OF EFFECTS	Don't know	Does not favor either the intervention or the comparison
RESOURCES REQUIRED	Large costs	The same as original
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Low	The same as original
COST EFFECTIVENESS	No included studies	Probably favors the comparison
EQUITY	Varies	The same as original
ACCEPTABILITY	Varies	The same as original
FEASIBILITY	Varies	The same as original

## TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	<b>Conditional recommendation against the intervention</b> ●	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

For asymptomatic women with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) suggests not using both digital breast tomosynthesis (DBT) and digital mammography (DM) in the context of an organised screening programme (conditional recommendation, very low certainty of the evidence).

## Justification

### Overall justification

To take the final decision the GDG considered what was decided for the recommendation on DBT vs DM (conditional for either), and the moderate undesirable effects and the larger costs.

### Detailed justification

#### *Undesirable Effects*

The undesirable effects considered for this recommendation are: interval breast cancer, overdiagnosis, radiation exposure. The GDG judged that they are moderate mainly because of the radiation dose that is doubled due to the use of both DBT and DM.

#### *Resources required*

The GDG judged that the resources required are large for screening using both DBT and DM. The resource considerations will also vary greatly based on the healthcare setting and health system funding for countries with universal healthcare coverage as compared to settings where DBT will be implemented in private healthcare settings. The GDG expressed their concern that this may lead to increased health inequities with varied implementation in different countries across Europe.

#### *Cost effectiveness*

Indirect evidence used for the recommendation on DBT vs DM suggest that the cost-effectiveness is in favour of DM alone.

## Subgroup considerations

Women with high mammographic breast density are likely to benefit most from the increased detection capability of DBT. The GDG developed a specific recommendation for this subgroup on the use of DBT in addition vs DM alone in the context of an organised screening programme.

## Implementation considerations

- Evidence will be emerging from ongoing and future breast cancer screening trials on DBT that may influence the current recommendation.
- Inappropriate worry about radiation dose should be dealt with in case programmes that are using the DBT in addition to DM combination. In general, the GDG believes it is important to educate women and health professionals on the risk of radiation in the context of possible benefits of screening.
- There will be significantly increased data storage needs for screening programmes using DBT in addition to DM as compared DM alone.

- Additional time is needed for radiologists to read tomosynthesis images, and therefore even more for the DBT in addition to DM examination compared to DM alone.
- The GDG noted that health equity in access to screening should be considered due to different resource settings and the capacity for different countries to pay for DBT in addition to DM over DM alone.

## Monitoring and evaluation

- Quality control/standardisation of the technology for better image storage should be undertaken.
- Standards should be developed for the image quality of tomosynthesis.
- In case DBT+DM is used in some pilot, screening monitoring and evaluation programs should be able to distinguish test done with DBT and with DM, stratified standard indicators should be computed.

## Research priorities

- The currently included studies only present data from first round DBT in addition to DM screening studies, thus the effects for several patient-important outcomes, which need a longer follow-up period, could not be taken into account. Research on several screening rounds of DBT in addition to DM are warranted.
- Further research is needed to build the evidence on benefits and harms of DBT in addition to DM compared to DM alone through comparison of direct outcomes, including impacts of interval cancer detection, stage of breast cancer at detection and mortality reduction or projection of mortality reduction (i.e. modelling starting from incidence of advanced stages and interval cancer).
- Further research information on harms of DBT in addition to DM, including rates of overdiagnosis of breast cancer, are warranted.
- Research investigating the cost-effectiveness of a breast cancer screening programme using DBT in addition to DM is needed to inform decision-making on breast cancer screening.
- Research is needed to define the quality parameters that would need to be fulfilled for breast cancer screening programmes that decide to use DBT in addition to DM.
- Evidence on implementation challenges of screening programmes already using DBT in addition to DM should be collected. To do that, screening programs should be able to produce stratified indicators (see monitoring and evaluation considerations)
- Research regarding distribution of tumour grade/biology/prognostic measures in the additionally detected cancers might help in clarifying the amount of possible overdiagnosis.