



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 Evidence profile

Healthcare question	Should screening using digital breast tomosynthesis vs. digital mammography be used in organised screening programmes for early detection of breast cancer in asymptomatic women?
Date	January 2020
Authors	Guideline Development Group (GDG): Mariangela Autelitano, Bettina Borisch, Mireille Broeders, Xavier Castells, Edoardo Colzani, Jan Daneš, Stephen Duffy, Patricia Fitzpatrick, Markus Follmann, Livia Giordano, Paolo Giorgi Rossi, Axel Gräwingholt, Solveig Hofvind, Lydia Ioannidou-Mouzaka, Susan Knox, Miranda Langendam, Annette Lebeau, Helen McGarrigle, Lennarth Nyström, Elsa Pérez Gómez, Cecily Quinn, Holger Schünemann, Alberto Torresin, Ruben Van Engen, Cary Van Landsveld-Verhoeven, Sue Warman, Kenneth Young. Systematic Review team: Carlos Canelo-Aybar, Jessica Beltran, Ingrid Arévalo-Rodríguez, Ignacio Ricci, Ivan Solá, Nieves Plana, Margarita Posso, David Rigau, Pablo Alonso-Coello. JRC Healthcare Quality team: Elena Parmelli, Zuleika Saz-Parkinson
Abbreviations	CI: Confidence interval RR: Risk ratio

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Digital breast tomosynthesis	Digital mammography	Relative (95% CI)	Absolute (95% CI)		
Breast cancer detection ^a												
10 1,2,3,4,5,6,7,8,9,10	observational studies ^{b,c}	serious ^d	not serious	not serious	not serious	none	1569/195336 (0.8%)	1357/236693 (0.6%)	RR 1.36 (1.22 to 1.51)	206 more per 100,000 (from 126 more to 292 more)	⊕⊕⊕○ MODERATE	CRITICAL
Breast cancer stage (inferred from invasive cancer detection rate)												
5 ^{1,5,6,7,9}	observational studies ^{b,c}	serious ^d	not serious	not serious	not serious ^e	none	522/82281 (0.6%)	626/134788 (0.5%)	RR 1.34 (1.19 to 1.51)	158 more per 100,000 (from 88 more to 237 more)	⊕⊕⊕○ MODERATE	CRITICAL
Invasive cancer /total cancer												
5 ^{1,5,6,7,9}	observational studies	serious ^d	not serious	not serious	not serious	none	522/646 (80.8%)	626/752 (83.2%)	RR 0.96 (0.66 to 0.97)	3 fewer per 100 (from 28 fewer to 2 fewer)	⊕⊕⊕○ MODERATE	
Breasr cancer detection (second round screening with DM alone after a first round of DBT or DM												
1 ^{11,f}	observational studies	serious ^d	not serious	not serious	not serious	none	103/26474 (0.4%)	254/45543 (0.6%)	RR 0.70 (0.56 to 0.88)	167 fewer per 100,000 (from 245 fewer to 67 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
False positive recall for assessment ^g												
10 1,2,3,4,5,6,7,8,9,10	observational studies ^{b,c}	serious ^d	very serious ^h	not serious	not serious	none	5685/193664 (2.9%)	10303/235138 (4.4%)	RR 0.80 (0.66 to 0.97)	876 fewer per 100,000 (from 1,490 fewer to 131 fewer)	⊕○○○ VERY LOW	CRITICAL

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Digital breast tomosynthesis	Digital mammography	Relative (95% CI)	Absolute (95% CI)		
Interval breast cancer ⁱ												
8 11,12,13,14, 15,16,17,18	observational studies ^b	serious ^d	not serious	not serious	very serious ^j	none	324/317913 (0.1%)	478/466253 (0.1%)	RR 1.04 (0.90 to 1.20)	4 more per 100,000 (from 10 fewer to 21 more)	⊕○○○ VERY LOW	CRITICAL
Radiation exposure												
3 ^{4,19,20}	observational studies ^b	not serious	not serious ^k	not serious ^l	not serious	none	Radiation doses for DBT vary by manufacturer and protocol (Bernardi 2016, Paulis 2015, Wallis 2012). _m			⊕⊕○○ LOW	CRITICAL	
Breast cancer mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Quality of life - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Radiation induced cancers-related to radiation dose - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Other causes of mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

Explanations

- Calculated as the total number of women with positive screening/overall number of screening examinations
- Cohort studies provided partial diagnostic information. The risk of bias was assessed using an ad-hoc modified QUADAS-2 tool
- Hofvind 2019 was a randomised prospective trial
- 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.
- Downgraded due to scarce number of events
- Hovda Radiology 2019 was included to assess detection rate outcome evaluated in a second round screening.
- Calculated as the number of false positives/overall number of screening examinations - total number of cancers
- Important unexplained heterogeneity (I²=97%)
- Calculated as the number of false positives/overall number of screening examinations - total number of cancers
- Wide 95%CI and low number of events
- Results were consistent independently of the technology used (Hologic Selenia Dimensions or Siemens Mammomat Inspiration).

- l. Radiation exposure is a surrogate outcome of "other cancer related to radiation".
- m. Doses levels are known to vary (diagnostic reference levels are typically country/region and system specific).

References

1. Houssami, N, Lockie, C, Pridmore, T, Taylor, M, Marr. Pilot trial of digital breast tomosynthesis (3D mammography) for population-based screening in BreastScreen Victoria. 2019.
2. Skaane P, Bandos, N, Niklason, S, Sebuødegård, Ø, Østerås, G, Gullien, G, Gur, H, Hofvind. Digital Mammography versus Digital Mammography Plus Tomosynthesis in Breast Cancer Screening: The Oslo Tomosynthesis Screening Trial. Radiology; 2019.
3. 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. From double reading of 2D mammography to single reading of tomosynthesis. Eur Radiol; 2018.
4. 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.
5. Hofvind S, Holen H, Hildegunn Houssami, Sebuødegård M, Moger H, Haldorsen A, Akslen. Two-view digital breast tomosynthesis versus digital mammography in a population-based breast cancer screening programme (To-Be): a randomised, controlled trial. Lancet Oncol; 2019.
6. Hofvind S, Hovda T, Holen Å, Lee C, Albertsen J, Bjørndal H, et al. Digital Breast Tomosynthesis and Synthetic 2D Mammography versus Digital Mammography: Evaluation in a Population-based Screening Program. Radiology; 2018.
7. 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.
8. 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.
9. 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.
10. Caumo, F., Zorzi, M., Brunelli, S., Romanucci, G., Rella, R., Cugola, L., Bricolo, P., Fedato, C., Montemezzi, S., Houssami, N.. Digital Breast Tomosynthesis with Synthesized Two-Dimensional Images versus Full-Field Digital Mammography for Population Screening: Outcomes from the Verona Screening Program. Radiology; 2017.
11. 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.
12. Bernardi D, Gentilini, De Nisi, Pellegrini, Fanto, Valentini, Sabatino, Luparia, Houssami. 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. The Breast; 2019.
13. 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.

14. 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.
15. Houssami, N., Bernardi, D., Caumo, F., Brunelli, S., Fanto, C., Valentini, M., Romanucci, G., Gentilini, M. A., Zorzi, M., Macaskill, P.. Interval breast cancers in the 'screening with tomosynthesis or standard mammography' (STORM) population-based trial. *Breast*; 2018.
16. 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.
17. Skaane, P., Sebuodegard, S., Bandos, A. I., Gur, D., Osteras, B. H., 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.
18. 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.
19. 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.
20. Paulis LE, Lobbes 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.