



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 tailored screening with hand-held ultrasound (HHUS) based on high mammographic breast density, in addition to mammography, vs. mammography alone be used for early detection of breast cancer in asymptomatic women?</b>	
<b>POPULATION:</b>	asymptomatic women, with high mammographic breast density and negative mammography in screening
<b>INTERVENTION:</b>	tailored screening with hand-held ultrasound (HHUS) based on high mammographic breast density, in addition to mammography,
<b>COMPARISON:</b>	mammography alone
<b>MAIN OUTCOMES:</b>	breast cancer mortality, stage of breast cancer, interval cancer rate, breast cancer detection rate, recall rate, rate of mastectomies, provision of chemotherapy, adverse effects,
<b>SETTING:</b>	European Union
<b>PERSPECTIVE:</b>	Population (National Health System)
<b>BACKGROUND:</b>	<p>Breast cancer is the second most commonly diagnosed cancer in the world (1.67 million cases diagnosed in 2012) and ranks as the fifth cause of death from cancer overall (522 000 deaths in 2012) (Ferlay 2012).</p> <p>Screening programmes play a crucial role in early breast cancer detection; they can increase the chance of survival as well as reduce disease specific mortality. Mammography remains the best method to detect breast cancer in an early stage. However, mammography has a lower sensitivity and specificity in women with radiologically dense breasts (Gilbert 2015). The use of different screening strategies including other imaging modalities, in addition to mammography, might improve early detection of breast cancer in women with higher mammographic breast density.</p> <p>Dense breast tissue is made up mostly of ductal structures and connective tissue, while non-dense breast tissue is mostly fatty. Breast density is seen only on mammograms.</p> <p>Due to lack of evidence using the breast density BIRADS (Breast Imaging Report and Database System) classification edition 5, the ECIBC's Guidelines Development Group (GDG) decided to base the recommendation on the previous breast density BIRADS classification assuming that the results are comparable for the two versions. Therefore, for the purpose of this clinical guideline, one of the following criteria classifies as dense breast:</p> <p>(1) BIRADS category scale: III-IV score.</p>

	<p>(2) For studies reporting quantitative percent density, a dense area of 50% as roughly equivalent to BIRADS III-IV (BIRADS III would be 50-75% and BI-RADS IV would be greater than 75%).</p> <p>(3) For those studies reporting the old Wolfe categories: BIRADS III would be P2 and BIRADS IV corresponding DY.</p>
<b>CONFLICT OF INTEREST:</b>	<p><u>Management of Conflicts of Interest (Col):</u> Cols for all Guidelines Development Group (GDG) members were assessed and managed by the European Commission Joint Research Centre (JRC) following an established procedure in line with the institutional rules. GDG member participation in the development of the recommendations was restricted, according to Col disclosure. Consequently, for this particular question, the following GDG members were recused from voting: Bettina Borisch, Roberto d'Amico, Chris de Wolf, and Axel Gräwingholt. Solveig Hofvind, Peter Rabe, Holger Schünemann, Alberto Torresin, Ruben van Engen, and Cary van Landsveld-Verhoeven were restricted from voting, as a preventive measure, as the Col information was not provided, but after its provision it was assessed and no Col were found. Miranda Langendam was not allowed to vote due to the established rules for external experts.</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>Breast cancer ranks as the fifth cause of death from cancer overall (522 000 deaths in 2012) and while it is the most frequent cause of cancer death in women in less developed regions (324 000 deaths), it is now the second cause of cancer death in more developed regions (198 000 deaths) after lung cancer (1).</p> <p>Breast cancer screening with additional screening modalities might improve the early detection of breast cancer in women with mammographically dense breast tissue. Although digital mammography (DM) has become an accepted standard of care in screening and diagnosis of breast cancer, up to 30% of breast cancers are not detected by standard screening (2). This percentage is even higher in women with dense breasts and in women under 50 years of age (Gilbert 2015). In women with dense breasts, risk of breast cancer is increased (3), and cancers may be masked and missed on mammography due to superposition of tissue; as a result, there might be an excess of late-stage disease (stages II and III) (4).</p>	<p>The GDG prioritised this question for the ECIBC.</p>

### Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE						ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ Trivial</li> <li>○ Small</li> <li>○ Moderate</li> <li>○ Large</li> <li>○ Varies</li> <li>● Don't know</li> </ul>	Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		<p>The included studies did not assess the outcomes of: breast cancer mortality, stage of breast cancer, interval cancer rate, rate of mastectomies, provision of chemotherapy or adverse effects including radiation exposure, radiation induced cancers-related to radiation dose (although these would be unaffected by the addition of ultrasound), overdiagnosis related adverse effects, false positive related adverse effects.</p> <p>There is a clear increase in cancer detection with the addition of HHUS. However, the anticipated effects on mortality, cancer stage and interval cancer rate are not known as the studies included did not examine these outcomes. Therefore, the GDG agreed that overall desirable anticipated effects are not known.</p>
					Risk with mammography alone	Risk difference with tailored screening with hand-held ultrasound (HHUS) based on high mammographic breast density, in addition to mammography,	
	Breast cancer detection rate	72998 (1 RCT) <sup>1</sup>	⊕⊕⊕○ MODERATE <sup>a</sup>	RR 1.54 (1.22 to 1.95)	Study population		
					324 per 100,000	175 more per 100,000 (71 more to 308 more)	

	Breast cancer detection rate	70942 (5 observational studies) <sup>2,3,4,5,6,b</sup>	⊕⊕○○ LOW	OR 1.50 (1.23 to 1.82) <sup>c,d</sup>	Study population	
					626 per 100,000 <sup>b</sup>	<b>310 more per 100,000</b> (143 more to 507 more)
	Breast Cancer Mortality - not reported	-	-	-	-	-
	Stage of breast cancer - not reported	-	-	-	-	-
	Interval cancer rate - not reported	-	-	-	-	-
	Recall rate - not reported	-	-	-	-	-
	Rate of mastectomies - not reported	-	-	-	-	-
	Provision of chemotherapy - not reported	-	-	-	-	-
	Adverse effects - not reported	-	-	-	-	-
	<ol style="list-style-type: none"> <li>Ohuchi N, Suzuki A, Sobue T, Kawai M, Yamamoto S, Zheng YF, et al. Sensitivity and specificity of mammography and adjunctive ultrasonography to screen for breast cancer in the Japan Strategic Anti-cancer Randomized Trial (J-START): a randomised controlled trial. Lancet; 2016.</li> <li>Corsetti V, Ferrari A, Ghirardi M, Bergonzini R, Bellarosa S, Angelini O, et al. Role of ultrasonography in detecting mammographically occult breast carcinoma in women with dense breasts. Radiol Med; 2006.</li> <li>De Felice C, Savelli S, Angeletti M, Ballesio L, Manganaro L, Meggiorini ML, et</li> </ol>					

	<p>al. Diagnostic utility of combined ultrasonography and mammography in the evaluation of women with mammographically dense breasts. J Ultrasound; 2007.</p> <p>4. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology; 2002.</p> <p>5. Korpraphong P, Limsuwarn P, Tangcharoensathien W, Ansusingha T, Thephamongkhon K, Chuthapisith S. Improving breast cancer detection using ultrasonography in asymptomatic women with non-fatty breast density. Acta Radiol; 2014.</p> <p>6. Venturini E, Losio C, Panizza P, Rodighiero MG, Fedele I, Tacchini S. Tailored breast cancer screening program with microdose mammography, US, and MR Imaging: short-term results of a pilot study in 40-49-year-old women. Radiology; 2013.</p> <p>a. Asymptomatic women aged 40-49 years from Japan (57,7% were classified as BI-RADS 3-4). Results for women with dense breast will be reported in the near future (PMID 26547101).</p> <p>b. Median or mean of the control group of the included studies as appropriate unless otherwise specified.</p> <p>c. Relative effect was adjusted for paired design.</p> <p>d. Incremental cancer detection was 380 cancers per 100,000 (from 166 more to 690 more ).</p>	
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## Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE					ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ Large</li> <li>○ Moderate</li> <li>○ Small</li> <li>○ Trivial</li> <li>○ Varies</li> <li>● Don't know</li> </ul>	Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	<p>There is only indirect evidence about the undesirable anticipated effects. There is uncertainty on the recall rates and the process used to recall women in the evidence presented.</p> <p>GDG members pointed out that the difficulty in comparing recall rates as if the addition of HHUS in those with dense breasts takes place at the same screening visit, there is no recall, but the screenee still undergoes additional imaging.</p> <p>Therefore, the GDG agreed that overall undesirable anticipated effects are not known.</p>
	Breast cancer detection rate	72998 (1 RCT) <sup>1</sup>	⊕⊕⊕○ MODERATE <sup>a</sup>	RR 1.54 (1.22 to	<div>Risk with mammography alone</div> <div>Risk difference with tailored screening with hand-held ultrasound (HHUS) based on high mammographic breast density, in addition to mammography,</div>	

			1.95)	324 per 100,000	<b>175 more per 100,000</b> (71 more to 308 more)
Breast cancer detection rate	70942 (5 observational studies) <sup>2,3,4,5,6,b</sup>	⊕⊕○○ LOW	<b>OR 1.50</b> (1.23 to 1.82) <sup>c,d</sup>	Study population	
				626 per 100,000 <sup>b</sup>	<b>310 more per 100,000</b> (143 more to 507 more)
Breast Cancer Mortality - not reported	-	-	-	-	-
Stage of breast cancer - not reported	-	-	-	-	-
Interval cancer rate - not reported	-	-	-	-	-
Recall rate - not reported	-	-	-	-	-
Rate of mastectomies - not reported	-	-	-	-	-
Provision of chemotherapy - not reported	-	-	-	-	-
Adverse effects - not reported	-	-	-	-	-
1. Ohuchi N, Suzuki A,Sobue T,Kawai M,Yamamoto S,Zheng YF,et al. Sensitivity and specificity of mammography and adjunctive ultrasonography to screen for breast cancer in the Japan Strategic Anti-					

	<p>cancer Randomized Trial (J-START): a randomised controlled trial. Lancet; 2016.</p> <ol style="list-style-type: none"> <li>2. Corsetti V, Ferrari A, Ghirardi M, Bergonzini R, Bellarosa S, Angelini O, et al. Role of ultrasonography in detecting mammographically occult breast carcinoma in women with dense breasts. Radiol Med; 2006.</li> <li>3. De Felice C, Savelli S, Angeletti M, Ballesio L, Manganaro L, Meggiorini ML, et al. Diagnostic utility of combined ultrasonography and mammography in the evaluation of women with mammographically dense breasts. J Ultrasound; 2007.</li> <li>4. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology; 2002.</li> <li>5. Korpraphong P, Limsuwarn P, Tangcharoensathien W, Ansusingha T, Thephamongkhon K, Chuthapisith S. Improving breast cancer detection using ultrasonography in asymptomatic women with non-fatty breast density. Acta Radiol; 2014.</li> <li>6. Venturini E, Losio C, Panizza P, Rodighiero MG, Fedele I, Tacchini S. Tailored breast cancer screening program with microdose mammography, US, and MR Imaging: short-term results of a pilot study in 40-49-year-old women. Radiology; 2013.</li> </ol> <ol style="list-style-type: none"> <li>a. Asymptomatic women aged 40-49 years from Japan (57,7% were classified as BI-RADS 3-4). Results for women with dense breast will be reported in the near future (PMID 26547101).</li> <li>b. Median or mean of the control group of the included studies as appropriate unless otherwise specified.</li> <li>c. Relative effect was adjusted for paired design.</li> <li>d. Incremental cancer detection was 380 cancers per 100,000 (from 166 more to 690 more ).</li> </ol>	
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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>		<p>The GDG members rated the overall certainty of the evidence of the effects as low because breast cancer detection rate (a critical outcome) was rated as low quality evidence.</p>



## 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>No specific studies focusing on HHUS 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 HHUS, as both screening tests are associated with similar desirable and undesirable effects (e.g. false positive findings or overdiagnosis). 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 (<i>low confidence</i>). However, these were not investigated specifically in relation to the potential outcomes from HHUS in addition to mammography. Also, they do not specifically apply to this population, of women informed of increased risk due to density and offered additional imaging as a result.</p>	<p>The GDG members agreed that there is important uncertainty or variability in the value people place in the main outcomes.</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 members agreed that there is no direct information available about the recall and biopsy rates. There is some indirect information showing that HHUS may possibly lead to an increase in the recall rate.</p> <p>As agreement was not reached, voting was conducted among GDG members: 5 members voted that the balance between desirable and undesirable effects "probably favours the intervention"; 8 members voted they "don't know".</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>The incremental cost per woman examined of including HHUS in addition to mammography in screening is EUR 59.1 or EUR 61.2, depending on whether women recalled and undergoing surgical biopsy were treated as an outpatient (local anaesthesia) or an inpatient (general anaesthesia) (2000-2007 year value) (5) .</p>	<p>Most of the models show smaller estimates per breast cancer detected.</p> <p>However, opportunistic vs organised screening programmes have varied costs.</p> <p>The GDG members noted that substantial differences could be observed in European countries with different screening policies and based on differences in the costs of labour depending on the country context.</p> <p>There are increased costs in HHUS associated with a near doubling of the radiologist's time.</p> <p>The GDG members considered indirect evidence: The lifetime incremental cost for biennial screening with supplemental HHUS is USD 560 per woman aged 50-74 years in the USA ( USD 411 Purchasing Power Parities (PPP) for the EU28) (2013 year value) (6).</p> <p>As agreement was not reached, voting was conducted among GDG members: 2members voted "moderate costs"; 11 members voted "large costs".</p>

## 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>	<p>The included studies were based on observational data conducted in the USA and Italy.</p>	<p>Results from the USA are qualified by the fact that single reading is the standard in the USA, whereas double reading is usually the policy in Europe.</p>

## Cost effectiveness

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <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>	<p>Incremental cost-effectiveness ratio ( ICER ) per cancer detected: The ICERs showed large variations across studies ranging from EUR 6 123 (7), EUR 14 618 (5), and EUR 19 158 (8). The variation in the ICERs is a result of the difference in the numbers of additional cancers detected with DM plus HHUS (N: 12, 37 and 2, respectively).</p>	<p>The GDG looked at indirect evidence coming from the USA where the ICER per Quality-Adjusted Life Year (QALY) gained by adding ultrasonography to digital mammography screening was UD 238 550 PPP (EU28) (2013 year value) (6).</p> <p>The costs and effects observed in the study of Sprague et al. (6) may not be transferable to European settings due to the differences between screening programmes.</p>

## 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>	<p>No systematic reviews on this topic was not carried out by DATE</p>	<p>The GDG took the view that there may be increased inequity with respect to implementation across Europe. Also, within programmes there may be policy decisions to restrict the programme, if there are increased costs and inability to fund universal participation. There are country level differences, and possible differences within a country, They can depend on who performs the screening as, particularly in HHUS the quality of the ultrasound depends greatly on who performs it.</p> <p>As agreement was not reached, voting was conducted among GDG members: 10 members voted health equity would "probably be reduced" and 4 members voted "varies".</p>

## 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>No specific studies considering the use of HHUS in addition to the standard regimen were identified.</p> <p>However, a systematic review (JRC Technical Report PICO 16-17, contract FWC443094032016; available upon request) found a number of barriers associated with breast cancer screening with mammography. See reviews of mammography screening for details.</p>	<p>The GDG members acknowledged that the fact that HHUS is being already used in certain settings is evidence that it is probably acceptable. The GDG members felt it would be very acceptable to <u>women</u>, as HHUS –in addition to standard screening has no radiation exposure and the physical discomfort associated with mammography would not be increased as a result of HHUS. <u>Payers</u> may not find it acceptable due to larger costs for low to moderate increases in breast cancer detection rates. The GDG members felt that, although the equipment for HHUS is probably already present in hospitals, more personnel time would be needed to carry out the procedures. As agreement was not reached, voting was conducted among GDG members: 6 members voted the acceptance would "vary"; 8 members voted "probably yes".</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>The GDG members took the view that the feasibility to implement the intervention will differ by country. In many settings HHUS in addition to the standard regimen is already being used or implemented (France, Austria, Czech Republic). However, GDG members from other countries (Spain, Italy) expressed the view it would be impossible to implement in an organised screening programme.</p> <p>The GDG members were of the opinion that the feasibility of implementation depends on the training of the radiologist. There were organisational concerns due to resources required to implement HHUS for screening. It would be difficult to implement this new organisational model without a great increase in the radiologist resources involved.</p>

## SUMMARY OF JUDGEMENTS

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

## TYPE OF RECOMMENDATION

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

### Recommendation

For asymptomatic women, with high mammographic breast density and a negative mammography, in the context of an organised screening programme, the ECIBC's Guidelines Development Group (GDG) suggests not implementing tailored screening with hand-held ultrasound (HHUS) over mammography screening alone, where such is not already the practice (conditional recommendation, low certainty of the evidence).

### Justification

*The decision was made based on consensus of the GDG members, with no voting necessary.*

The conditional recommendation (rather than strong) against tailored screening with hand-held ultrasound (HHUS) in addition to mammography screening over mammography screening alone in women with high mammographic breast density, in the context of an organised screening programme, is the result of a balance of the health effects that does not favour either the intervention nor the comparison, in the context of low certainty in the evidence about these effects, and the large resource (cost) associated with HHUS. There is an improved detection rate of HHUS plus mammography over mammography alone, however, this improvement is smaller as compared to alternative imaging modalities such as DBT (see recommendation for this intervention) although no direct comparison of HHUS and DBT was made.

In settings that are not already using HHUS in tailored screening, it is likely not useful to implement this for screening programmes

### Subgroup considerations

The only subgroup assessed in this recommendation was women with high mammographic breast density.

### Implementation considerations

If resources and implementation are not a concern, or where HHUS has already been implemented, countries may decide to keep HHUS-based screening programmes.

The GDG members felt that information and education for women about mammographic breast density is critical. The opinion of women regarding HHUS depends on the quality of the information provided to them with regards to the evidence behind this modality for tailored screening, including the information concerning the limitations or uncertainty about the effects of HHUS and inter-operator variability.

The GDG expressed concern about the quality assurance for HHUS in contexts where training is variable and screening is opportunistic and not organised. No new technology would likely be necessary in most settings, although some institutions may not have the ultrasound equipment which fulfils the requirements for performing breast ultrasound.

There are additional training requirements for radiologists performing HHUS.

Pressure to implement HHUS exists, which may have to be considered with regards to the conditional recommendation against based on the evidence reviewed by the GDG.

## Monitoring and evaluation

Quality assurance of HHUS appears challenging to conduct or implement. In settings where they decide to implement HHUS, the GDG members recommends consideration be given to quality assurance of HHUS.

## Research priorities

None were considered by the GDG members.

## REFERENCES SUMMARY

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