Annals of Internal Medicine

CLINICAL GUIDELINE

Breast Cancer Screening and Diagnosis: A Synopsis of the European Breast Guidelines

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Description: The European Commission Initiative for Breast Cancer Screening and Diagnosis guidelines (European Breast Guidelines) are coordinated by the European Commission's Joint Research Centre. The target audience for the guidelines includes women, health professionals, and policymakers.

Methods: An international guideline panel of 28 multidisciplinary members, including patients, developed questions and corresponding recommendations that were informed by systematic reviews of the evidence conducted between March 2016 and December 2018. GRADE (Grading of Recommendations Assessment, Development and Evaluation) Evidence to Decision frameworks were used to structure the process and minimize the influence of competing interests by enhancing transparency. Questions and recommendations, expressed as strong or conditional, focused on outcomes that matter to women and provided a rating of the certainty of evidence.

Recommendations: This synopsis of the European Breast Guidelines provides recommendations regarding organized screening programs for women aged 40 to 75 years who are at average risk. The recommendations address digital mammography screening and the addition of hand-held ultrasonography, automated breast ultrasonography, or magnetic resonance imaging compared with mammography alone. The recommendations also discuss the frequency of screening and inform decision making for women at average risk who are recalled for suspicious lesions or who have high breast density.

Ann Intern Med. doi:10.7326/M19-2125 **Annals.org**

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This article was published at Annals.org on 26 November 2019.

Despite intensified efforts by the European Council since 2003, the implementation of organized, population-based mammography screening is not uniform across Europe and depends greatly on the policies in place in different countries, the organization of health care, and available resources (1). Since the last edition of the European Guidelines on Breast Cancer Screening and Diagnosis was published in 2006 (2), new evidence regarding breast cancer and innovation in guideline methodology prompted the European Commission Initiative on Breast Cancer (ECIBC) to develop new evidence-based recommendations (in short, the European Breast Guidelines).

This article provides a synopsis of 15 key recommendations selected from the European Breast Guidelines, coordinated by the European Commission's Joint Research Centre and developed by an international guideline development group (GDG). These guidelines inform women, health professionals, and policymakers about important questions related to organized mammography screening and breast cancer diagnosis, but recommendations may apply in contexts in which organized screening programs are not in place. The recommendations primarily address women at average risk for breast cancer without increased risk due to genetic predisposition (mutations in *BRCA1* and *BRCA2*), reproductive history, or race/ethnicity. However, women with a family history, who may have a higher-than-average risk, are included in the ECIBC recommendations. Some recommendations also focus on women with high breast density and suspicious lesions on screening. The corresponding evidence reviews and recommendations are kept up to date and are available for adoption and adaptation at https://ecibc.jrc.ec.europa.eu/recommendations.

Guideline Development and Review Process

The European Commission adheres to methods for producing trustworthy guidelines (3–6), which we described in detail previously (7). In brief, the European Commission authorized new systematic reviews, or syntheses of existing ones, up to March 2016 for earlier recommendations and to December 2018 for later, more recent recommendations. This evidence informed the criteria in the GRADE (Grading of Recommendations Assessment, Development and Evaluation) Evidence to Decision (EtD) frameworks that the GDG, guided by 4 cochairs and vice chairs, used to develop the recommendations (7–10). Each recommendation is

See also:

Editorial comment

Web-Only
Supplement

* For members of the ECIBC Contributor Group, see the **Supplement** (available at Annals.org).

linked to the full online EtD containing references, explanations (including considerations for implementation, monitoring, and research priorities), and judgments that were developed with GRADE's official app GRADEpro (www.gradepro.org) (7).

RECOMMENDATIONS

The **Supplement Table** (available at Annals.org) lists all 40 questions and recommendations addressed by the group as of May 2019; the first 15 recommendations listed in the table are those addressed in this synopsis. The table includes the strength (strong or conditional) and certainty-of-evidence ratings and the dates of the last pertinent literature searches. The GDG took a programmatic population perspective, suggesting that strong recommendations in this context may be adopted as policies in most situations (11). Conditional recommendations suggest that policymaking will require substantial debate and involvement of various stakeholders. The implications of the recommendations for women and clinicians are supported by more specific, linked recommendations focusing on communication and shared decision making.

Should Organized Mammography Screening in Women Be Used?

The GDG considered women in the following age groups: 40 to 44, 45 to 49, 50 to 69, and 70 to 74 years. Evidence from some systematic reviews applied to all age groups for 1 or more EtD criteria. For example, mammography screening does not seem to create anxiety in women who are given a clear result after a mammogram. However, women recalled for further testing reported transient or long-term anxiety (from 6 months to 3 years after recall), but this was not consistent across studies (12–14). Women generally consider these undesirable effects acceptable (low certainty of evidence), and a systematic review suggested that women place a relatively low value on the psychosocial and physical effects of false-positive results and overdiagnosis; however, some studies raised concerns about whether women fully understand the resulting implications (15).

Organized Mammography Screening in Women Aged 40 to 44 Years or 45 to 49 Years

Recommendation 1. For asymptomatic women aged 40 to 44 years with an average risk for breast cancer, the ECIBC's GDG suggests not implementing organized mammography screening (conditional recommendation, moderate certainty of evidence; EtD available at http://bit.ly/2pf8l9M).

Recommendation 2. For asymptomatic women aged 45 to 49 years with an average risk for breast cancer, the ECIBC's GDG suggests mammography screening over no mammography screening, in the context of an organized screening program (conditional recommendation, moderate certainty of evidence; EtD available at http://bit.ly/2Pn1HZx).

Eight randomized controlled trials (RCTs) of invitation to mammography screening provided breast cancer mortality data from 348 478 women younger than 50 years (16–22), and 4 reviews of observational studies evaluated relevant outcomes (12–14, 23). Organized mammography screening probably reduces breast cancer mortality (16–22) and may reduce the risk for breast cancer stage IIA or higher (17, 18, 22, 24–28). The incidence of breast cancer and mortality increases with age, and the GDG extrapolated that the absolute health benefits are greater in women aged 45 to 49 than those aged 40 to 44 years.

Data from 5 available trials in women aged 40 to 74 years suggest an increase in the rate of mastectomy (19, 29–32), although the GDG was concerned that these results might be misleading because of lead time. One RCT suggests a rate of 12.4% (95% CI, 9.9% to 14.9%) to 22.7% (CI, 18.4% to 27.0%) for overdiagnosis, depending on whether a population or an individual woman perspective is taken (27). The number of false-positives depends on the age of first screening, and women aged 40 to 44 years also have a greater radiation risk than older women.

The balance of desirable versus undesirable health effects for starting screening at age 40 probably favors no screening (the GDG judged that the undesirable health effects are large and the desirable ones small). However, for the 45- to 49-year age group, the higher breast cancer incidence and mortality compared with women between the ages of 40 and 44, as well as observational evidence showing a greater benefit in this age group (33), led the GDG to judge that the balance of health effects probably favors screening, although the required resources for screening likely differ across settings (34, 35).

Organized Mammography Screening in Women Aged 50 to 69 Years

Recommendation 3. For asymptomatic women aged 50 to 69 years with an average risk for breast cancer, the ECIBC's GDG recommends mammography screening over no mammography screening, in the context of an organized screening program (strong recommendation, moderate certainty of evidence; EtD available at http://bit.ly/2qNKE91).

On the basis of data from 249 930 women aged 50 to 69 years from 6 RCTs, invitation to organized mammography screening reduces breast cancer mortality (17, 19–22, 36) and may reduce the risk for breast cancer stage IIA or higher (17, 22, 24–26, 37). Five trials describe increased rates of mastectomy in women between ages 40 and 74 (19, 29–32), with concerns about lead-time bias similar to those for the younger age group. Pooled estimates from 2 RCTs suggest overdiagnosis rates of 10.1% (CI, 8.6% to 11.6%) and 17.3% (CI, 14.7% to 20.0%) (37, 38).

The cost-effectiveness studies probably favored screening, but this would vary across countries (34, 39–41). The GDG determined that screening in this age group has a net health benefit, and other EtD criteria were generally in favor of implementing organized mammography screening. Thus, despite uncertainty about the relative importance of outcomes or values,

the GDG made a strong recommendation for organized screening but emphasizes that all invited women should receive clear information about the desirable and undesirable effects to make informed decisions.

Organized Mammography Screening in Women Aged 70 to 74 Years

Recommendation 4. For asymptomatic women aged 70 to 74 years with an average risk for breast cancer, the ECIBC's GDG suggests mammography screening over no mammography screening, in the context of an organized screening program (conditional recommendation, moderate certainty of evidence; EtD available at http://bit.ly/31KjCMA).

According to 2 RCTs of invitation to mammography screening in 18 233 women aged 70 years and older (19, 21), organized mammography screening reduces breast cancer mortality, the risk for breast cancer stage IIA or higher, and detection of tumors larger than 50 mm (25).

Five trials in women aged 40 to 74 years described increased mastectomy rates (19, 29–32). Concerns have been raised about lead-time bias, the small number of women aged 70 to 74 years included for the outcome of mastectomy, and the available data for overdiagnosis being derived exclusively from women aged 50 to 69 years for an overall judgment of probable net health benefit. Other EtD criteria also were generally in favor of implementing organized mammography screening in this age group.

How Often Should Women Attend an Organized Mammography Screening Program?

Women Aged 45 to 49 Years

Recommendation 5. For asymptomatic women aged 45 to 49 years with an average risk for breast cancer, the ECIBC's GDG suggests either biennial or triennial mammography over annual screening in the context of an organized screening program (conditional recommendation, very low certainty of evidence; EtD available at http://bit.ly/32O1faP).

Women Aged 50 to 69 Years

Recommendations 6 and 7. For asymptomatic women aged 50 to 69 years with an average risk for breast cancer, the ECIBC's GDG recommends against annual mammography screening (strong recommendation, very low certainty of evidence; EtD available at http://bit.ly/2BlzNzj) and suggests biennial mammography screening over triennial mammography screening in the context of an organized screening program (conditional recommendation, very low certainty of evidence; EtD available at http://bit.ly/31QCUQi).

Women Aged 70 to 74 Years

Recommendations 8 and 9. For asymptomatic women aged 70 to 74 years with an average risk for breast cancer, the ECIBC's GDG recommends against annual mammography screening (strong recommendation, very low certainty of evidence; EtD available at http://bit.ly/342qJS0) and suggests triennial mammography screening over biennial mammography screening in the context of an organized screening program (conditional recommendation, very low certainty of evidence; EtD available at http://bit.ly/2JpK1su).

The GDG compared annual, biennial, and triennial screening intervals in women for whom the GDG either strongly (ages 50 to 69 years) or conditionally (ages 45 to 49 and 70 to 74 years) recommended screening (Table 1). Evidence exists from RCTs to compare annual with triennial screening in women aged 50 to 69 years (42) and from observational studies (43–46) for a broader age range. To fill gaps in the direct evidence, the GDG used evidence from indirect comparisons of annual (18, 20, 47) or biennial (19, 48) screening compared with no screening, as well as the results of modeling studies (44, 49, 50). The GDG also conducted its own simple modeling—for example, calculating events by subtracting the estimated outcome rates in women aged 45 to 69 years (or 70 to 74 years) from those aged 50 to 69 years (or 70 to 74 years)—and assumed that effects were incremental to those found for women aged 50 to 69 years (or 70 to 74 years) at screening.

The benefits resulting from more rather than less frequent screening differed across age groups but suggest that for all age groups, annual screening may reduce breast cancer mortality compared with biennial or triennial screening. Compared with biennial screening, the incidence of stage IIB to IV breast cancer and interval cancer seemed lower with annual screening (51–53). More quality-adjusted life-years seemed to be gained with annual than biennial or triennial screening (44, 49). When biennial was compared with triennial screening, the reported benefits were similar in all age groups, except for detection of stage IIB to IV breast cancer in women aged 50 to 69 years, which favored biennial screening.

Harms also differed across age groups but showed similar patterns. Annual screening showed increased overdiagnosis rates, more false-positive results (in some comparisons, >30% more), and more suggestions for follow-up with biopsies for false-positive results (in some comparisons, >5% more) across age groups compared with biennial or triennial screening (43, 44, 49, 52, 54). Biennial screening probably leads to more overdiagnosis, false-positive results, and suggestions for follow-up with biopsies for false-positive results than triennial screening, but the differences become smaller with increasing age (44, 45). Radiation-induced breast cancer and higher rates with biennial or triennial screeningof radiation-induced breast cancer deaths probably result from annual (6 in 100 000 women) and biennial screening (4 in 100 000 women) compared with triennial screening (50).

What Tests Should Be Used to Screen for Breast Cancer?

The following 2 recommendations about digital breast tomosynthesis (DBT), originally made in April

Table 1. Multiple-Intervention Comparison of Desirable and Undesirable Consequences of Annual, Biennial, and Triennial Mammography Screening for Women Aged 45 to 49, 50 to 69, and 70 to 74 Years

Evaluation Criteria	Screening Intervals for Women Aged 45 to 49 Years		
	Annual vs. Triennial	**Triennial vs. Biennial**	**Annual vs. Biennial**
Certainty of evidence	Very low	Very low	Very low
Balance of health effects	Probably favors triennial screening	Probably favors biennial screening	Probably favors biennial screening
Resources required	Large costs	Moderate savings	Moderate costs
Cost-effectiveness	Probably favors triennial screening	Probably favors triennial screening	Probably favors biennial screening
Equity	Varies	Varies	Varies
Acceptability	Varies	Varies	Varies
Feasibility	Varies	Yes, compared with biennial	Varies
Overall judgment	The GDG judged that biennial or triennial screening provided the most net desirable consequences compared with annual screening. Biennial screening probably provides more net desirable health consequences than triennial, but costs are lower for triennial screening programs.		

	Screening Intervals for Women Aged 50 to 69 Years	
	Annual vs. Triennial	**Triennial vs. Biennial**
Certainty of evidence	Very low	Very low
Balance of health effects	Probably favors triennial screening	Probably favors biennial screening
Resources required	Large costs with annual screening	Moderate savings with biennial screening
Cost-effectiveness	Does not favor either	Does not favor either
Equity	Varies	Varies
Acceptability	Varies	Varies
Feasibility	Probably no, compared with triennial	Yes, compared with biennial
Overall judgment	The GDG judged that the net desirable consequences of annual screening are much smaller than those of triennial screening, largely because of the harms from more frequent screening (a strong recommendation against annual screening resulted). The GDG judged that triennial screening has less net desirable consequences than biennial, but the panel was not as certain (a conditional recommendation resulted). The GDG decided by logic that biennial also has more net desirable consequences than annual screening, and it did not produce a detailed EtD framework.	

	Screening Intervals for Women Aged 70 to 74 Years		
	Annual vs. Biennial	**Annual vs. Triennial**	**Triennial vs. Biennial**
Certainty of evidence	Very low	Very low	Very low
Balance of effects	Probably favors biennial screening	Probably favors triennial screening	Does not favor either the intervention or the comparison
Resources required	Large costs with annual	Moderate costs with annual	Moderate savings with triennial
Cost-effectiveness	Favors biennial	No included studies	Probably favors triennial
Equity	Varies	Varies	Varies
Acceptability	Probably no, compared with biennial	Probably no, compared with triennial	Probably yes, compared with biennial
Feasibility	Probably no, compared with biennial	Probably no, compared with triennial	Yes, compared with biennial
Overall judgment	The GDG judged that biennial and triennial screening provide similar net desirable consequences and both of these intervals have more net desirable consequences than annual screening intervals.		

EtD = Evidence to Decision; GDG = guideline development group.

2016, were updated and changed in November 2018.

Should Screening With DBT (Including Synthesized 2-Dimensional Images) Versus Digital Mammography Be Used for Early Detection of Breast Cancer in Asymptomatic Women?

Recommendation 10. For asymptomatic women with an average risk for breast cancer, the ECIBC's GDG suggests screening with digital mammography over DBT, in the context of an organized screening program (conditional recommendation, very low certainty of evidence; EtD available at http://bit.ly/2pRtw1G). Because the GDG made a strong recommendation for screening at ages 50 to 69 years, this applies specifically to this age group.

We found 9 relevant observational studies (55–63), but they did not measure the outcomes of breast cancer mortality, cancer stage, and quality of life. Screening with DBT increased breast cancer detection compared with digital mammography (55–57, 61, 62). No differences in interval cancer detection rate, recall rate, or false-positive recall were found between DBT and digital mammography (55–58, 61–63).

The resources needed to move to DBT were considered moderate by the GDG, not only because of the greater costs of the machines but also because of the human resources required. One observational study (59) reported that radiologists' reading time would double for DBT compared with digital mammography, but staff costs may vary depending on the country. The GDG emphasized that research on direct outcomes (namely, other-cause mortality, breast cancer mortality, radiation-induced cancer, and quality of life) is not yet available, leading to uncertainty in the balance of health effects from using DBT in screening programs.

Should Screening Using DBT (Including Synthesized 2-Dimensional Images) in Addition to Digital Mammography Versus Digital Mammography Alone Be Used for Early Detection of Breast Cancer in Asymptomatic Women?

Recommendation 11. For asymptomatic women with an average risk for breast cancer, the ECIBC's GDG suggests screening with digital mammography alone over screening with DBT in addition to digital mammography, in the context of an organized screening program (conditional recommendation, very low certainty of evidence; EtD available at http://bit.ly/33aQf6V).

We found 1 RCT (64) and 10 observational studies (55–60, 65–71) that were relevant. Screening with DBT in addition to digital mammography increased the cancer detection rate and detection of invasive cancer compared with digital mammography alone (55–58, 64–66, 69). No differences were found in recall rate (55, 56, 58, 64–66, 69), but in 4 of the observational studies the rate of false-positive recalls was increased when both techniques were combined, although the RCT (64) showed no differences. The GDG agreed that the effect would vary depending on the baseline rate. Despite about a 2-fold increase in radiation dose with use of both DBT and digital mammography, the GDG determined that the absolute increase in radiation-induced cancer was probably small (58–60, 64).

The resources needed to adopt DBT plus digital mammography were considered large because of the higher costs of the machines and the necessary human resources (72). For instance, radiologists' reading time would at least double by using both techniques (77 to 191 seconds) compared with digital mammography alone (33 to 67 seconds) (56, 59, 73). Although the GDG could not determine whether using DBT in addition to digital mammography in screening programs provided a net health benefit, it concluded that, overall, the undesirable consequences were greater than the desirable ones.

What Tests Should Be Used to Screen for Breast Cancer in Women With Dense Breast Tissue?

The GDG answered 4 questions about whether a woman whose mammogram shows no breast cancer but who has dense breast tissue should have another mammogram or other tests, such as DBT, magnetic resonance imaging (MRI), or ultrasonography (automated or hand-held). The DBT question currently is being updated, so only the other 3 questions are described in detail here.

Tailored Screening With Automated Breast Ultrasonography

Recommendation 12. For asymptomatic women with high mammographic breast density and negative mammography results, in the context of an organized screening program, the ECIBC's GDG suggests not implementing tailored screening with automated breast ultrasonography (ABUS) over mammography screening alone (conditional recommendation, very low certainty of evidence; EtD available at http://bit.ly/341Kg4V).

We found 3 observational studies reporting the effect on breast cancer detection and recall rates of additional screening with ABUS after a negative mammography result (74–76). The addition of ABUS after a negative mammography result increased the number of breast cancer cases detected. However, interaction may exist between risk factors other than breast density and detection rate; therefore, absolute or relative effects may not be comparable. The GDG expressed concern about the link between higher detection rate and mortality because of the lack of evidence for the outcome of breast cancer mortality. Two studies suggested an increase in recall rate with ABUS (74, 75). The GDG determined that the balance of health effects favors neither ABUS after mammography nor mammography alone, and other EtD criteria generally were in favor of not implementing additional screening with ABUS.

Tailored Screening With Hand-Held Ultrasonography Based on High Mammographic Breast Density

Recommendation 13. For asymptomatic women with high mammographic breast density and a negative mammography result, in the context of an organized screening program, the ECIBC's 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 evidence; EtD available at http://bit.ly/366cEVx).

Additional screening with HHUS after a negative mammography result increased the number of breast cancer cases detected compared with mammography alone in 1 randomized and 5 observational studies (77–82). Because of a lack of evidence about the anticipated effects on mortality and other outcomes, the GDG could not determine what the desirable effects would be.

We found no evidence of undesirable effects of adding HHUS after a mammogram. The GDG considered indirect evidence suggesting that the lifetime incremental cost for biennial screening with supplemental HHUS is $560 per woman aged 50 to 74 years and the incremental cost-effectiveness ratio per quality-adjusted life-year gained is equal to $238 550 in purchasing power parity in the United States (83). The GDG determined that the balance of health effects favors neither HHUS after mammography nor mammography alone, so the additional resources needed to implement HHUS led the GDG to advise against adding HHUS for these women.

Tailored Screening With MRI Based on High Mammographic Breast Density

Recommendation 14. For asymptomatic women with high mammographic breast density and a negative mammography result, in the context of an organized screening program, the ECIBC's GDG suggests not implementing tailored screening with MRI over mammography screening alone (conditional recommendation,

Table 2. Recommendations for Breast Cancer Screening for Average-Risk Women*

Guideline, Year (Reference)	Age, *y*	Direction and Strength of the Recommendation (if Provided)	Age to Stop Screening Mammography	Screening Interval
ACOG, 2017 (99)	40 (discuss; offer if chosen by SDM) 50–74 (start screening if not previously started)	Discuss and offer if chosen In favor	75 y	Every 1 or 2 y
ACP, 2019 (100)†	40–49 50–74	No recommendation made, only discussion should be held Offer screening	75 y with life expectancy <10 y	Every 2 y
ACS, 2015 (101)	40–44 (discuss; offer if chosen by SDM) 45 (start screening)	Discuss and offer if chosen In favor	Life expectancy <10 y	Every 1 y for age 45–54 y and every 2 y for age ≥55 y
ACR, 2017 (102)	40 (start screening)	In favor	None	Every 1 y
NCCN, 2018 (103)	40 (start screening)	In favor	None	Every 1 y
WHO, 2014 (104)	50–75	In favor	75 y	Every 2 y
USPSTF, 2016 (105)	40–49 50–75	Discuss and offer if chosen In favor	75 y	Every 2 y
CTFPHC, 2018 (106)‡	40–49 50–69 70–74	Suggest against Suggest in favor Suggest against	75 y	Every 2–3 y
ECIBC, 2019	40–45 45–49 50–69 70–74	Suggest against‖ Suggest in favor‖ Recommend‖ Suggest in favor, organized mammography screening‖	74 y	Not applicable§ Every 2–3 y Every 2 y Every 3 y

ACOG = American College of Obstetricians and Gynecologists; ACP = American College of Physicians; ACR = American College of Radiology; ACS = American Cancer Society; CTFPHC = Canadian Task Force on Preventive Health Care; ECIBC = European Commission Initiative on Breast Cancer; NCCN = National Comprehensive Cancer Network; SDM = shared decision making; USPSTF = U.S. Preventive Services Task Force; WHO = World Health Organization.
* Modified and updated from Qaseem and colleagues (100).
† The ACP did not produce a guideline but a guidance statement; no systematic reviews were conducted, but existing guidelines were reviewed to formulate ungraded statements rather than recommendations.
‡ The CTFPHC guideline addressed only women aged 40–74 y.
§ If implemented, follow recommendations for women aged 45–49 y, every 2–3 y.
‖ SDM should take place in organized programs, applicable to all ECIBC recommendations.

very low certainty of evidence; EtD available at http://bit.ly/32PMDaK).

We found 5 observational studies reporting on rates of breast cancer detection and recall (84–88). Additional testing with MRI markedly increased the breast cancer detection rate compared with mammography alone, raising concerns about overdiagnosis; no evidence was found for mortality or other related outcomes. The GDG discussed the importance of false-positives and interval cancer cases in particular, as well as possible side effects of the contrast medium used in MRI-based screening.

Although the GDG found no evidence regarding resources and cost-effectiveness, it assumed that the costs of MRI equipment and examinations are much higher than those of digital mammography. The GDG determined that MRI after mammography in women with high mammographic breast density probably results in net harm, and after also considering the increased costs, the group advised against additional testing with MRI for these women.

What Test Should Be Used for Diagnosis in Average-Risk Women Recalled Because of Suspicious Lesions at Mammography Screening?

Recommendation 15. The ECIBC's GDG suggests using DBT over diagnostic mammography projections in women at average risk for breast cancer recalled for suspicious lesions at mammography screening (conditional recommendation, moderate certainty of test accuracy data; EtD available at http://bit.ly/31KV0mD).

We found 10 studies (72, 89–97) reporting the accuracy of DBT compared with assessment mammography for diagnosis in women recalled because of suspicious lesions at mammography screening. Digital breast tomosynthesis leads to more true-positives (patients correctly diagnosed with breast cancer), fewer false-negatives (patients incorrectly classified as not having breast cancer), more true-negatives (women without breast cancer), and fewer false-positives (women incorrectly assumed to have breast cancer). Although the GDG found no evidence regarding the consequences of these accuracy results on clinical outcomes, the group discussed the possible concern about radiation dose in DBT. Only 1 study reported radiation dose (a surrogate outcome to assess the risk for radiation-induced breast cancer), and the GDG judged that side effects of DBT compared with assessment mammography (including magnification) were likely to be trivial (91).

The GDG concluded that DBT probably confers a net health benefit, and although the DBT device is much more expensive than the equipment needed for magnification mammography, information for other EtD criteria also generally favored using DBT for diagnosis in women recalled for suspicious lesions at mammography screening.

DISCUSSION

In developing the European Breast Guidelines, the ECIBC used a rigorous approach to produce recommendations on breast cancer screening and diagnosis for women. The guidelines include recommendations that address the use of various tests, including DBT, MRI, ABUS, and HHUS, for women who have suspicious lesions on mammography screening or who have dense breast tissue. The use of some tests, such as DBT, in women with high breast density are not addressed in this synopsis, but updates that incorporate emerging pertinent evidence and related recommendations are under way.

The strengths of the guidelines include their adherence to requirements for trustworthy development (4, 6, 98), including the public and transparent display of all evidence, considerations, and judgments for use by women, health care professionals, policymakers, and researchers (https://ecibc.jrc.ec.europa.eu/recommendations). Previously we described limitations of our guidelines related to the lack of high-certainty evidence for some recommendations, the absence of formal modeling, conflicts of interest, and process issues (7). We believe these limitations are balanced by the recommendations' transparency, which allows for scientific discourse and comparison with other guidelines.

Table 2 shows that our key recommendations on screening in women younger than 50 years generally agree with guidelines from the American College of Obstetricians and Gynecologists (99), American College of Physicians (100), and American Cancer Society (101), which suggest shared decision making. However, our recommendations are less strong and favor wider screening intervals than those of the American College of Radiology (102) and the National Comprehensive Cancer Network (103) (Table 2). For the other age groups, the recommendations agree with those of the World Health Organization (104) and U.S. Preventive Services Task Force (105) but not with those of the Canadian Task Force for Preventive Health Care (CTFPHC) (106). The CTFPHC also used the GRADE EtD approach, allowing a more detailed exploration of the differences. The key difference is the CTFPHC's recommendation against screening in women until age 49 and after age 69. We believe this is a result of the CTFPHC attaching a higher value to potential harms; more concerns about risk of bias, leading to lower certainty of the evidence; and greater importance attached to outcomes for which less information was available. This in turn led the CTFPHC to assign overall lower certainty. The ECIBC's GDG carefully analyzed the existing data and supplemented the RCTs when available with observational studies, and had no serious concerns about risk of bias in the trials overall (see explanations in the evidence profile at http://bit.ly/2qNKE91). In contrast to the CTFPHC, the ECIBC's GDG also did not have concerns about inconsistency in trial results, making the GDG more confident in the recommendation for women aged 50 to 69 years.

The feasibility of implementing a recommendation, the acceptability of that recommendation, the required resources, and the associated values are often context dependent. Some countries have started or intend to adapt or adopt specific recommendations in Europe (Bulgaria, Czech Republic, Denmark, Estonia, Germany, Italy, Norway, and Slovakia) and outside Europe (Bahrain, Chile, China, and Tunisia) using the EtD frameworks and the GRADE-ADOLOPMENT (GRADE EtD frameworks for adoption, adaptation, and de novo development of trustworthy recommendations) methodology (107).

In summary, this synopsis presents and summarizes the rationale for 15 key recommendations of the European Breast Guidelines. The complete set of recommendations (Supplement Table) provides advice on additional issues, such as how to communicate with vulnerable populations about screening options, how to inform women about results, the use of decision aids, how to work up calcifications, whether to use clip marking for core needle biopsies, and whether mammograms require double reading.

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Acknowledgment: The authors thank Jesús López Alcalde who coordinated the JRC methods for the ECIBC guidelines between 2013 and 2016, Chris de Wolf, Roberto D'Amico, and Peter Rabe for their contributions to the ECIBC guidelines as previous Joint Research Centre colleagues or retired GDG members.

Financial Support: By the European Commission.

Disclosures: Members of the GDG do not receive financial compensation for their work but are reimbursed by the European Commission for travel-related expenses for the meetings organized by the Joint Research Centre. Dr. Schünemann reports that the European Commission had chosen to use GRADE as one of the core methods for its guidelines before involving Dr. Schünemann. He was invited to participate in the guideline development as a methodologist and was elected

by the ECIBC GDG as its cochair. He is also cochair of the GRADE working group and has codeveloped its methodology and tools, was commissioned by the National Academy of Sciences to write the background reports for the Institute of Medicine standards for trustworthy guideline development with coauthors, has conducted Cochrane reviews (currently is director of Cochrane Canada), and is a member of the Board of Trustees of the Guidelines International Network. He has not received direct financial payments for ECIBC work but has received travel support and is under contract from the European Commission for a project relating to other guideline methods. Dr. Quinn is the chair of the European Working Group for Breast Screening Pathology (EWGBSP). Various companies have provided some sponsorship to the EWGBSP for group meetings. Dr. Alonso-Coello reports that his institution received payments from the European Commission to develop the systematic reviews informing the recommendations. He coordinated the systematic review team informing the guidelines. He is a member of the GRADE guidance group of the GRADE working group and a member of the board of the Guidelines International Network. He has contributed to the development of some of the methodology and tools. Dr. Giorgi Rossi reports that he published opinions about the superiority of public, organized, population-based screening programs instead of opportunistic and private screening, according to the European Commission recommendations 2003/878/EC. He is on the steering committee of MyPeBS (My Personal Breast Screening), a European multicentric trial to compare the effectiveness of personalized screening programs and standard protocols, and of the RETomo and MAITA trials, comparing digital mammography and DBT in breast cancer screening. Dr. Lebeau reports grants and reimbursement for travel-related expenses related to consultancy from Roche Pharma and Novartis Oncology, and grants from BioNTech Diagnostics, outside the submitted work. Dr. Lebeau reports that she is chair of the Breast Pathology Working Group of the German S3 Guidelines for the Early Detection, Diagnosis, Treatment and Follow-up of Breast Cancer; a member of the Scientific Advisory Council for the Cooperation Alliance Mammography (Kooperationsgemeinschaft Mammographie GBR), Germany; a member of the certification commission "breast cancer centres" as a representative of the German Society of Pathology and the Federal Association of German Pathologists; and a board member of the German Society of Pathology. Dr. Hofvind reports permanent employment as a researcher at the Cancer Registry of Norway, independent of her job as administrative leader of BreastScreen Norway. Dr. Canelo-Aybar reports that his institution received payments from the European Commission to develop the systematic reviews informing the recommendations. He is a member of the GRADE Working Group. Dr. Sardanelli is responsible for the department of radiology performing mammographic screening at the IRCCS Policlinico San Donato, Milan, Italy. He is a member of the executive board of the European Society of Breast Imaging and codirector of the Breast MRI training course run by this society; director of the European Network for Assessment of Imaging in Medicine, joint initiative of the European Institute for Biomedical Imaging Research; editor-in-chief of *European Radiology Experimental*; and a recipient of research grants from Bracco, Bayer, and General Electric. Dr. Sardanelli is not a member of the GDG but did participate in formulating the recommendations. Dr. Parmelli is employed by the European Commission. Dr. Gräwingholt is head of the mammography screening center Paderborn, consultant radiologist for screening programs in Switzerland, and consultant radiologist for Hellenic School of Senology. Dr. Saz-Parkinson is employed by the European Commission, coordinating the ECIBC's GDG. Authors not named here have disclosed no conflicts of interest. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum= M19-2125.

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