



**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

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*Should triennial vs. biennial mammography screening be used for early detection of breast cancer in women aged 50 to 69?*

## RECOMMENDATION

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***For asymptomatic women aged 50 to 69 with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) suggests biennial mammography screening over triennial mammography screening in the context of an organised screening programme (conditional recommendation, very low certainty in the evidence).***

# ASSESSMENT

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<b>POPULATION</b>	early detection of breast cancer in women aged 50 to 69
<b>INTERVENTION</b>	triennial
<b>COMPARISON</b>	biennial mammography screening
<b>MAIN OUTCOMES</b>	Breast cancer mortality; Stage of breast cancer (IIB-IV); QALYs; Interval cancer; False positive; Biopsy recommendation; Overdiagnosis; Radiation induce breast cancer/Death.
<b>SETTING</b>	Europe Union.
<b>PERSPECTIVE</b>	Population (National Health System).
<b>BACKGROUND</b>	<p>Breast cancer is the second most common cancer in the world and the most frequent cancer among women with an estimated 1.67 million new cancer cases diagnosed in 2012 (25% of all cancers) (Ferlay et al., 2013). In 2018 in, Europe, it is estimated that 250,682 women between the ages of 50 and 69 will be diagnosed with breast cancer and 50,568 will die (Ferlay, 2018). Mammography screening has both potential benefits and harms. The Guidelines Development Group has strongly recommended in favour of screening women between the ages of 50 and 69. Debate about the recommended interval for screening with mammography remains due to the theoretical advantage of earlier diagnosis but a potential increase in harms with shorter screening intervals. For example, the National Health Service Breast Screening Programme (NHSBSP) recommends screening every three years for women aged 50 to 70, the USPSTF recommended screening every two years for women aged 50 to 69 (Siu, 2016), while the ACS recommended annual screening between ages 45 to 54 years and every two years from age 55 and older (Myers, 2015).</p> <p>Management of Conflicts of Interest (Col): ColS for all Guidelines Development Group (GDG) members were assessed and</p>

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 CoI disclosure. Consequently, for this particular question, the following GDG members were recused from voting: Roberto d'Amico and Chris de Wolf. Miranda Langendam, as external expert, was also not allowed to vote, according to the ECIBC rules of procedure. For more information please visit <http://ecibc.jrc.ec.europa.eu/gdg-documents>

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## JUDGEMENTS

### ***Is the problem a priority?***

- ☐ No
- ☐ Probably no
- ☐ Probably yes
- ☒ Yes
- ☐ Varies
- ☐ Don't know

Breast cancer is the second most common cancer in the world and, by far, the most frequent cancer among women with an estimated 1.67 million new cancer cases diagnosed in 2012 (25% of all cancers) (Ferlay et al., 2013). Breast cancer ranks as the fifth cause of death from cancer overall (522,000 deaths) and it is the second cause of cancer death in developed regions (198,000 deaths, 15.4%) after lung cancer. In 2018 in, Europe, it is estimated that 250,682 women between the ages of 50 and 69 will be diagnosed with breast cancer and 50,568 will die (Ferlay, 2018). Breast cancer is the fourth cancer with the highest disease burden (Tsilidis et al., 2016).

Although mammography screening is generally accepted as beneficial in reducing breast cancer mortality in women 50-69 years. The balance between benefits and harms for the different screening intervals is still debatable, with recommended periodicity varying between annual to triennial.

### ***Additional considerations***

This question was prioritised by the GDG.



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***How substantial are the desirable anticipated effects?***

- ☐ Trivial
- ☒ Small
- ☐ Moderate
- ☐ Large
- ☐ Varies
- ☐ Don't know

***Additional considerations***

In a systematic review for the Canadian Task Force on Preventive Health Care: based on indirect evidence from different RCTs for women in the age range of 50-69 years the risk of breast cancer mortality compared to no screening, for a screening interval <24 mo (4 studies) was RR 0.86 (95%CI 0.75-0.98); and for a screening interval ≥24 mo (3 studies) was RR 0.67 (95%CI 0.51-0.88) (Care, 2011).

From the Swedish two county trial, with an average screening interval of 35 months in women 50 years and older; the percentage of interval cancers during the first 12 months after the last mammogram was 13%, from 12 to <24 months was 29% and at ≥24 months it was 45% (Tabár, 1987)

From a report of the U.K. NHS Breast Screening Programme (triennial screening programme): in women aged 50-64 years the rate of interval cancers per 1,000 women screened was 0.55 for <12 months, 1.13 for 12 to <24 months and 1.22 for 24 to <36 months after last mammogram (Bennett, 2011).

The GDG discussed the fewer overdiagnosis, fewer false positives and fewer false positive biopsy recommendations with triennial screening

compared to biennial.

However, as agreement within the GDG for the desirable anticipated effects could not be reached, voting among the members without Col resulted in the following: 17 members voted in favour of "small" desirable anticipated effects, 2 members voted in favour of "moderate" desirable anticipated effects'

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***How substantial are the undesirable anticipated effects?***

- ☐ Large
- ☒ Moderate
- ☐ Small
- ☐ Trivial
- ☐ Varies
- ☐ Don't know

***Additional considerations***

The GDG agreed that the undesirable effects of triennial screening were moderate due to the fewer breast cancer deaths averted and fewer QALYs with triennial screening and the increased number of interval cancers.

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***What is the overall certainty of the evidence of effects?***

☒ Very low

***Additional considerations***

☐ Low

☐ Moderate

☐ High

☐ No included studies

The GDG agreed the overall certainty was very low as that was the lowest certainty of the critical outcomes described above.

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***Is there important uncertainty about or variability in how much people value the main outcomes?***

☐ Important uncertainty or variability

☒ Possibly important uncertainty or variability

☐ Probably no important uncertainty or variability

☐ No important uncertainty or variability

☐ No known undesirable outcomes

A systematic review (JRC Technical Report PICO 10-11, contract FWC443094012015; available upon request) shows that women place a low value on the psychosocial and physical effects of false positive results and overdiagnosis. However, women generally consider these undesirable effects acceptable (*low confidence*). These findings are of limited value mainly given the significant concerns regarding the adequacy of the information provided to the participants, in order to take an informed decision. Also, acceptability of false positive results is based on studies of patients who have already received a false positive result, whose preferences 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. Regarding breast cancer diagnosis, there is very limited data available on patients' views. One of the main themes identified in the literature is that patients 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 confidence*). Also, women have a higher overall preference towards more comfortable, brief diagnostic procedures (*low confidence*).

No specific studies neither focusing on the rest of the critical outcomes nor comparing different screening intervals were identified. The findings, all from mammography studies, however, are likely to be generalizable to facing the decision of selecting different mammography schedules, as all screening intervals are associated with similar desirable and undesirable effects (e.g. false positive findings or overdiagnosis).

***Additional considerations***

The GDG agreed by consensus that there is possibly important uncertainty in how much people value the main outcomes.

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***Does the balance between desirable and undesirable effects favor the intervention or the comparison?***

☐ Favors the comparison      ***Additional considerations***

☒ Probably favors the comparison

☐ Does not favor either the intervention or the comparison

☐ Probably favors the intervention

☐ Favors the intervention

☐ Varies

☐ Don't know

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The GDG agreed that the balance of the effects probably favours the comparison, biennial screening.

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***How large are the resource requirements (costs)?***

- ☐ Large costs
- ☐ Moderate costs
- ☐ Negligible costs and savings
- ☒ Moderate savings
- ☐ Large savings
- ☐ Varies
- ☐ Don't know

***Additional considerations***

Triennial screening was shown to have lower costs compared to biennial screening.

The GDG agreed by consensus that there would be moderate cost savings with triennial screening compared to biennial screening.

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***What is the certainty of the evidence of resource requirements (costs)?***

☒ Very low

☐ Low

☐ Moderate

☐ High

☐ No included studies

The quality of the evidence of resource requirements was very low due to study design (models were based on observational data), inconsistency, and indirectness.

Inconsistency in costs was due to differences in costs year value (2004, 2005 and 2012) and settings (costs reported in Slovenia were higher than in Spain). Costs and resources used in Spain and Slovenia may not be applicable to other European settings.

***Additional considerations***

The certainty according to the evidence presented was very low but the GDG was certain that biennial screening is more costly than triennial.

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

☐ Favors the comparison

***Additional considerations***

☐ Probably favors the comparison

☒ Does not favor either the intervention or the comparison

The GDG felt that the ICER presented had a narrow range of uncertainty. The cost of 25,517 and 50,304 Euros gained per one QALY doing biennial screening is at the limit of the willingness to pay threshold of most countries.

☐ Probably favors the intervention

☐ Favors the intervention

☐ Varies

☐ No included studies

However, as agreement within the GDG could not be reached, voting among the members without Col resulted in the following: 5 members voted that it "probably favours the comparison" and 14 members voted that it "does not favour either the intervention or the comparison".

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***What would be the impact on health equity?***

- ☐ Reduced
- ☐ Probably reduced
- ☐ Probably no impact
- ☐ Probably increased
- ☐ Increased
- ☒ Varies
- ☐ Don't know

No systematic review of the evidence was conducted.

***Additional considerations***

The GDG discussed that there would be reduced equity if you increase the period between screenings, because not all women would have an equitable screening opportunity, as it would depend on the existing protocol/resources in their setting. In situations where programmes are well implemented, changing from biennial to triennial screening may not affect particular subgroups of women.

On the other hand, in settings where already triennial screening is not reaching all women, of note low income women or women who are working, there may be even more challenges if they have to attend screening at increased frequencies (biennial screening). Therefore, in settings where reduced equity already exists, changing screening interval from triennial to biennial may further reduce equity.



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***Is the intervention acceptable to key stakeholders?***

- ☐ No  
☐ Probably no  
☐ Probably yes  
☐ Yes  
☒ Varies  
☐ Don't know

No systematic review of the evidence was conducted.

***Additional considerations***

The GDG felt that it would be very difficult to convince women, and healthcare providers that the interval should decrease from biennial to triennial screening. However, in contexts where programmes are not already in place, it would be possible to consider triennial screening.

Policy-makers: may not be willing to decrease screening interval if biennial is currently being used in their context.

However, as agreement within the GDG could not be reached, voting among the members without Col resulted in the following: 5 members voted that it is "probably not" acceptable to go from biennial to triennial screening, one member voted that it is "probably acceptable" and 11 members voted that it "varies"

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***Is the intervention feasible to implement?***

- ☐ No
- ☐ Probably no
- ☐ Probably yes
- ☒ Yes
- ☐ Varies
- ☐ Don't know

No systematic review of the evidence was conducted.

***Additional considerations***

The GDG felt that it would be feasible to implement a less frequent screening interval

## CONCLUSIONS

**Should triennial vs. biennial mammography screening be used for early detection of breast cancer in women aged 50 to 69?**

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
	○	⊗	○	○	○
RECOMMENDATION	For asymptomatic women aged 50 to 69 with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) suggests biennial mammography screening over triennial mammography screening in the context of an organised screening programme (conditional recommendation, very low certainty in the evidence).				
JUSTIFICATION	<p>Overall justification</p> <p>Agreement within the GDG could not be reached, so voting among the members without Col took place and resulted in the following: 12 members voted for a "Conditional recommendation against the intervention", 7 members voted for a "Conditional recommendation for either the intervention or the comparison"</p> <p>The GDG felt that the health effects probably favour biennial screening over triennial screening. There were moderate savings in doing triennial screening, however, neither was favoured with regards to cost effectiveness, but triennial screening was considered to be feasible.</p>				
SUBGROUP CONSIDERATIONS	None considered.				

## **IMPLEMENTATION CONSIDERATIONS**

The GDG felt that selection of the screening interval should be dependent on the resources available in a specific country, including the sustainability of the costs and resources available.

In contexts where screening programmes do not already exist, the GDG felt that it would be better to have a 3-year screening interval than no screening programme at all.

In contexts where a 3-year screening interval is currently used, the GDG recognised that human resource (radiologists/radiographers) availability may determine the decision.

## **MONITORING AND EVALUATION**

None considered.

## **RESEARCH PRIORITIES**

1. The GDG agreed that more research on the effectiveness of the different screening intervals, comparative studies, would be helpful due to the very low certainty of the evidence. 2. The GDG felt that the implications of breast density on appropriate screening intervals should be prioritised as this could be a risk modifier that may need different intervals. 3. The GDG discussed the need for improved knowledge on radiation dose and the differences that screening intervals would have on the radiation dose received by women. 4. The GDG felt that increased cost effectiveness data, having more contextualised costs and cost-effectiveness analysis and from other settings would be helpful for future recommendations; this included checking the consistency of cost-effectiveness models with new research from trials on breast cancer screening and natural history of breast cancer disease. Also many member states have cost analysis but they are in the grey literature and not publicly available, and this should be shared with the scientific community.