



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

Should triennial vs. biennial mammography screening be used for early detection of breast cancer in women aged 70 to 74?

RECOMMENDATION

For asymptomatic women aged 70 to 74 with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) suggests triennial mammography screening over biennial mammography screening in the context of an organised screening programme (conditional recommendation, very low certainty in the evidence).

ASSESSMENT

POPULATION

Mammography screening in women 70 years or older

INTERVENTION

triennial

COMPARISON

biennial mammography screening

MAIN OUTCOMES

Stage of breast cancer (IIB-IV); False positive results; Biopsy recommendation.

SETTING

European Union

PERSPECTIVE

Population (National Health System)

BACKGROUND

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 54,490 women between the ages of 70 and 74 will be diagnosed with breast cancer and 15,149 will die (Ferlay, 2018). The Guidelines Development Group has conditionally recommended in favour of screening for women between the ages of 70 and 74. However, there continues to be debate about the recommended interval for screening with mammography, particularly for ages 70 and above. Management of Conflicts of Interest (CoI): CoIs for all Guidelines Development Group (GDG) members were assessed and managed by the Joint Research Centre (JRC) following an established procedure in line with European Commission rules. GDG member participation in the development of the recommendations was restricted, according to 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>

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 54,490 women between the ages of 70 and 74 will be diagnosed with breast cancer and 15,149 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. In the group of women aged between 70 to 74, the amount of evidence is even more scarce and the topic controversial.

Additional considerations

This question was prioritised by the GDG.

How substantial are the desirable anticipated effects?

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

Additional considerations

For the modelling study, events were calculated by subtracting estimation of 50 to 74 screening years minus 50 to 69 screening years. Effects are then incremental to those observed in the 50 to 69 screening age group, and might vary by the year of last screening.

The GDG felt that the desirable effects are small. There are fewer false positives, fewer overdiagnosis, and fewer false positive biopsies with triennial screening.

How substantial are the undesirable anticipated effects?

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

Additional considerations

The GDG considered the 9 fewer breast cancer deaths averted and 28 fewer QALYs as small undesirable anticipated effects.

What is the overall certainty of the evidence of effects?

☒ Very low

Additional considerations

☐ Low

☐ Moderate

☐ High

☐ No included studies

There are no modelling studies that model these few years, so it was necessary to do the subtraction mentioned previously. This is why the GDG agreed that the quality of evidence of this data was very low.

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 generalisable 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 that there is possibly important uncertainty in how much people value the main outcomes.

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

The GDG agreed that the balance of effects did not favour either the intervention or the comparison.

☐ Probably favors the intervention

☐ Favors the intervention

☐ Varies

☐ Don't know

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.

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 considered 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. The study performed in Slovenia reported data for women aged 71 to 75 years.

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.

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 had some concerns about the variations around the ICER estimate.

☒ Probably favors the intervention

The GDG did not reach consensus on whether or not the cost-effectiveness evidence favoured the intervention, so voting took place among members without Col. 14 members voted "probably favours the intervention" and 4 members voted "favours the intervention".

☐ Favors the intervention

☐ Varies

☐ No included studies

Therefore, the GDG agreed the cost-effectiveness evidence probably favours the intervention.

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.

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 health care 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"

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 70 to 74?

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 70 to 74 with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) suggests triennial mammography screening over biennial mammography screening in the context of an organised screening programme (conditional recommendation, very low certainty in the evidence).				
JUSTIFICATION	<p>Overall justification</p> <p>As agreement within the GDG for direction of this recommendation could not be reached, voting among the members without CoI resulted in the following: ten members voted in favour of 'conditional recommendation for the intervention' and nine members voted in favour of 'conditional recommendation for either the intervention or the comparison'.</p> <p>The reasons for a conditional recommendation are the sustainability of the screening programme, the cost of the intervention and the resources available.</p>				
SUBGROUP CONSIDERATIONS					

IMPLEMENTATION CONSIDERATIONS

In countries where women have been screened for twenty years biennially and now they have to do triennial screening, this may not be acceptable and would require designing implementation strategies.

MONITORING AND EVALUATION

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. Due to the growing ageing population, the GDG believed women in the older age groups would need to have a longer follow-up in order to see how many breast cancers are detected at those ages. In addition, the GDG believed there was a need for more data on interval cancers in the varying screening intervals, as there is currently very little data on this. 3. 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. 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.
