



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 annual 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) recommends against annual mammography screening over biennial mammography screening, in the context of an organised screening programme (strong recommendation, very low certainty in the evidence).

ASSESSMENT

POPULATION

Mammography screening in women 70 years or older

INTERVENTION

annual

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

Undesirable effects

Based in two modelling studies annual interval had 2,307 to 7,100 more false positives cases than biennial interval per 100,000 women (*very low quality*); estimates for benign biopsies per 100,000 were for annual 0 to 142 more than biennial interval (*very low quality*) (Yaffe, 2015)(Vilapinyo, 2014).

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.

Differences between biennial or triennial versus annual screening is small and given no sensitivity analysis was carried out, the GDG considered that there would be no significant differences in the breast cancer deaths averted.

There is no real benefit in breast cancer deaths averted.

No difference in stage of breast cancer.

The GDG estimates 20 or less interval cancers over 100,000 women screened, from the breast cancer cases detected shown.

As the GDG could not reach an agreement, voting among GDG members with no CoI took place with the following results: 13 members voted "small" and 9 members voted "trivial".

How substantial are the undesirable anticipated effects?

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

Undesirable effects

Based in two modelling studies annual interval had 2,307 to 7,100 more false positives cases than biennial interval per 100,000 women (*very low quality*); estimates for benign biopsies per 100,000 were for annual 0 to 142 more than biennial interval (*very low quality*) (Yaffe, 2015)(Vilapinyo, 2014).

Additional considerations

The undesirable effects considered were the greater cases of overdiagnosis, false positive results and false positive biopsy recommendations, and fewer QALYs as a result of these three previous outcomes.

The GDG agreed the undesirable effects were moderate.

What is the overall certainty of the evidence of effects?

Very low

Low

Moderate

High

No included studies

Additional considerations

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

Probably favors the intervention

Favors the intervention

Varies

Don't know

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

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

The GDG agreed by consensus that the resource requirements were large.

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 annual screening is more costly than biennial screening.

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

This is a model performed in Slovenia. In this case, annual screening has 10 more QALYs than biennial screening, and it costs over 400,000 euros per QALY. So, according to the data previously discussed, with fewer QALYs with annual screening, we would have to pay even more.

Probably favors the intervention

Favors the intervention

Varies

No included studies

Therefore, using this model, and even in the most positive assumptions, the GDG agreed it would not be cost-effective.

The GDG agreed by consensus that the cost-effectiveness favours the comparison.

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 screening frequency (from biennial to annual), 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 annual screening may not affect particular subgroups of women.

In settings where already biennial 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.

In settings where reduced equity already exists, changing screening interval from biennial to annual may further reduce equity.

The GDG agreed by consensus equity would therefore vary.

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

Women – probably not acceptable to have annual screening due to having to attend the screening programmes more frequently, although some women may prefer annual screening.

Policy-makers: the GDG felt that they may not be willing to decrease the screening interval, particularly if biennial screening is currently being used in their context.

In addition, the radiologists of the GDG agreed that the acceptability would be low if there is more harm than benefit, taking into account the associated increased costs with doing annual screening.

Therefore, GDG agreed that most stakeholders would probably not find the intervention acceptable

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 agreed by consensus that it was probably not feasible to implement annual screening.

In areas where not even biennial or triennial screening is in place, it will be even more difficult to do it annually.

The GDG discussed the increased human resources needed as well as additional costs among the barriers to implementing annual screening in settings where this intervention is not currently in place.

CONCLUSIONS

Should annual 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	<p>For asymptomatic women aged 70 to 74 with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) recommends against annual mammography screening over biennial mammography screening, in the context of an organised screening programme (strong recommendation, very low certainty in the evidence).</p>				
JUSTIFICATION	<p>Overall justification</p> <p>The strong recommendation against annual screening was agreed by the GDG by consensus.</p> <p>The GDG agreed that the large costs of annual screening is what makes this recommendation strong, despite the very low certainty in the evidence.</p>				

SUBGROUP CONSIDERATIONS

IMPLEMENTATION CONSIDERATIONS

The GDG does not feel that annual screening programmes are currently in place in any jurisdictions in Europe and therefore there would be no implementation considerations for this strong recommendation

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. 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. This priority may apply to all other screening interval recommendations.
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