Reviewer’s report

Title: Breast cancer screening in the Czech Republic: time trends in performance indicators during the first seven years of the organised programme

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Reviewer: Karsten Juhl Jørgensen

Reviewer’s report:

The authors of this manuscript aim to quality-assess the Czech Republic organized mammography screening programme and state that:

‘The performance of the programme was assessed using the standard set of performance indicators introduced in European Guidelines.’

While this may seem reasonable, it is far from problematic. This is because both the principles of the European Guidelines, and indeed this manuscript, rely on surrogate markers for efficacy and safety and entirely disregard the effects of the most important harm of mammography screening: overdiagnosis of tumors that were not destined to be detected in the lifetime of the women, because they do not cause symptoms or require treatment.

Overdiagnosis is not mentioned at all in this manuscript, despite the fact that the quantification of this harm is one of the most intensely debated topics in the field of mammography screening. It is a harm that can challenge the justification of organised breast screening of any age group. There is no longer debate as to whether overdiagnosis occurs, only about the magnitude of the problem. Several recent papers in highly esteemed medical journals have highlighted this issue in the past few years, none of which are mentioned by the authors of this manuscript. A few of the most important ones are listed here:


It is therefore not correct when the authors state about their methods and results that:
'This promises effectiveness, safety and efficiency similar to randomized clinical trials, which justifies the enormous investment into programme initiation and operation.'

There were 30% overdiagnosis in the randomized trials, which means that 10 healthy women received an unnecessary diagnosis of breast cancer for every one woman who had her life extended (see: Gøtzsche PC, Nielsen M. Screening for breast cancer with mammography. Cochrane Database of Systematic Reviews 2009; Issue 4. Art. No.:CD001877.). It is an indefensible shortcoming not to mention this harm in a review of a breast cancer screening programme today. It is this harm of cancer screening that is a main reason we do not screen smokers for lung cancer with chest x-rays, and that many European countries do not recommend screening for prostate cancer with PSA. The authors correctly note that screening has increased breast cancer incidence markedly in the screened age groups in the Czech republic (see their figure 3), whereas it has been constant in non-screened age groups. This should sound the alarm bells of overdiagnosis, as there seems not to be any compensation for all those ‘early diagnoses’.

The fact that overdiagnosis is disregarded in this manuscript profoundly influence the results of the analyses presented. Overdiagnosis occur mainly of early stage cancers and increase their absolute number extensively. When the authors mention that the percentage of late stage cancer is decreasing, this is misleading, because it may simply reflect overdiagnosis of early stage disease. The main question is if the rate of late stage cancers decrease. If screening does not reduce the rate of late stage disease, it simply cannot work. It seems that this hasn’t happened in the Czech Republic, which is hardly surprising, as this is a general observation in countries with prolonged screening and high uptake. (see: Autier P, Boniol M, Middleton R, et al. Advanced breast cancer incidence following population based mammographic screening. Ann Oncol 2011; doi:10.1093/annonc/mdq633). This study is, however, published too late for the authors to have included it. What they should have noted is that breast cancer mortality has decreased more in non-screened age groups (women below age 50 years) than in screened age groups (50-69 years) in European countries with long-running breast screening programmes. This clearly show that treatment has had a major role in the overall reductions in breast cancer mortality in Europe that we have happily observed over the past 20 years, and it questions the role of mammography screening (see: Autier P, Boniol M, LaVecchia C, et al. Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. BMJ 2010; 341:c3620).

And other recent studies that have questioned the mortality reduction from screening are not mentioned either:
Indeed, the selection of references and the presentation of the expected benefit does not seem representative of the available evidence:

‘Efficacy of breast cancer screening by mammography in preventing breast cancer deaths (by 25-30%) was demonstrated in eight randomised controlled trials and several meta-analyses [4].’

This is misleading, as several of the trials demonstrated no effect, or a much smaller effect. The reference provided is to a review article (Schopper D, de Wolf C: How effective are breast cancer screening programmes by mammography? Review of the current evidence. Eur J Cancer 2009, 45:1916-1923). However, the two most comprehensive systematic reviews of the randomised trials, performed by independent researchers and following a risk of bias assessment based on empirical evidence, both reached quite different estimates of the benefit: about a 15% reduction, or half of the effect that was the estimate justifying the implementation of screening in many countries (see: the Cochrane review mentioned above, and: Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. Ann Intern Med 2009; 151:727-737, W237-742). The fact that even this reduced benefit has been questioned in several recent papers (see above) is not mentioned.

Also, the authors seem to have missed a fundamental premise for invitations to screening. They conclude their abstract with the statement:

‘Further stimulation of participation through invitation system is necessary to exploit the full potential of screening mammography at the population level’.

But invitations to screening must never ‘stimulate participation’. What they must stimulate is informed choice, with a clear statement that non-participation is as sensible a choice as participation. This is because of the small chance of benefit for the individual (a 1 in 2000 chance over 10 years of participation) and the risk of severe harm (the risk of overdiagnosis is 1 in 200 over 10 years). This pre-requisite of informed choice is not only mentioned in the European Guidelines, but also in national legislation.

This manuscript does not critically evaluate the Czech mammography screening programme. It sticks to guidelines that define substitute outcomes that are claimed to be quality assessment tools, yet does not consider the most important harm of the intervention. Further, basic assumptions for these quality measures are wrong and will lead to misleading conclusions about the safety and efficacy of screening. This manuscript therefore paints much too bright a picture of the Czech mammography screening programme. The authors are obliged to take the most important harm of the screening programme into account in their assessment. Anything else is indefensible and a disservice to screening participants.

Level of interest: An article of limited interest
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests