Reviewer's report

Title: Breast cancer screening: evidence of benefit depends on the method used

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Reviewer: Lennarth Nyström

Reviewer's report:

Autier and Boniol have reviewed the case-control and incidence-based mortality studies (IBM) to evaluate the effectiveness of the service-screening program with mammography and found them seriously biased. Thereafter they advocate the trend in advanced breast cancer is the only scientifically sound method.

Case-control method

The authors refer to papers by surveys by Flamant in France and Ferrante in US to elucidate the self-selection among participants. These studies are very weak support for self-selection first because they are based on self-reported participation in mammography, but mainly because they are performed in countries without an organised service-screening program with mammography including individual invitation to screening. Today France has a program, but not at the time of the survey. Further the US program is very different from the organised service-screening programs in the Nordic countries, the Netherlands, UK, Italy and Spain.

Further, the authors refer to papers by Duffy et al and Mook et al claiming that "before screening starts the risk of women likely to participate in screening is known to be 30% to 60% lower than that of women not likely to participate". I cannot find any support for that statement in their papers.

IBM studies

The whole section is confusing. The authors emphasize selection bias, but their selection of studies in the review of IBM studies obviously suffer from selection bias. No selection criteria is specified, some studies are overlapping (e.g. Tabar et al 2003 and SOSSEG 2006 as well as Sarkeala 2008 and Anttila 2008) in time and study are, no synthesis is made (meta-analysis). Kalager (2010) is included in spite of that the majority of the study counties were observed for such a short time that it would be impossible to detect any effect. Further one can question why no study from Spain (e.g. Ascunce 2007) or Italy (e.g. Paci 2002) were included?? The authors also accuse the studies from Finland and Sweden for "not assessing changes in mortality trends due to improved patient management", however, that was not the aim of any of the studies.

The comparison between the studies from Denmark and Norway is meaningless due to the weakness in the study from Norway as mentioned above.

The authors often draw parallels between the trend in the breast cancer mortality
and the outcome of the service-screening programs with mammography claiming that the observed decrease in the breast cancer mortality due to the service-screening program is not directly reflected in the breast cancer mortality trends. Let me remind the authors that the breast cancer deaths in 2011 consists of breast cancer cases diagnosed during the preceding 30-year period!!!!

The authors refer to the IARC handbook on Breast Cancer Screening where it was stated that "Routine screening programmes can be evaluated most readily by time trends and differential mortality from the disease for which screening is being performed". First of all the IARC Handbook is not a golden standard. I was involved in writing one of the chapters in the book. I can assure you that all epidemiologist that had been involved in the evaluation of cancer screening programs objected strongly to that statement, but the Editors did not listen to our arguments and refused to delete it.

Conclusion
The main problem is that the authors conclude about issues not discussed or supported in the paper.

Case-control studies
Where is the support for geographical variations in patient management? At least in the Nordic countries we have had national programs for breast cancer care....

IBM studies
"Main limitation is the paucity of population-based cancer registries...". Where can you find support for that. The Nordic Cancer Registries and known for their high quality data

IBM

Quality of written English: Acceptable

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

Declaration of competing interests:
I have no competing interests.