Reviewer's report

Title: Is there excess mortality in women screened with mammography? A meta-analysis of non-breast cancer mortality

Version: 1 Date: 24 July 2013

Reviewer: Brian Cox

Reviewer's report:

Major Compulsory Revisions

1. The discussion should be more focused on the issue of excess non-breast cancer mortality in the studies rather than false positives. Some discussion about the selection of subjects for invitation in the RCTs should be included. For example, were people with significant co-morbidity excluded. Certainly, those with previous breast cancer were excluded. Could randomisation by cluster (Kopparberg and Ostergotland, for example) rather than by individual produce different co-morbidity in the two arms of a trial and thus alter non-breast cancer mortality though to 13 years of follow-up. If relatively small adverse effects from screening were to take more than 13 years to manifest themselves, then excess non-breast cancer mortality from screening could eventuate later, but I can not think of an example that would. Could one argue that mammography screening should be even less likely to induce excess mortality now compared to when the RCTs were conducted or is the risk of overtreatment from overdiagnosis increased since the studies were conducted. Are there methods that could be used, other than the modelling suggested, that might answer the hypothesis that no excess non-breast cancer mortality is present in current service screening. Could a case-control study of adverse treatment effects shed any light on the effects of overtreatment in screening. These aspects might be included in the discussion.

2. Figure 1, 2 and 3 are hanging. That is, they are not referenced in the article where their results are discussed in the 'Results' section.

Minor Essential Revisions

1. The last section of the discussion

'Non-breast cancer related mortality may be increased by overdiagnosis and overtreatment.

Cancer treatments can cause many adverse effects (risks from surgery, chemotherapy, hormone therapy, and radiation therapy). [51, 52] Even low doses of radiation may cause cancer. [53]'

should come before false positive diagnosis and overtreatment are discussed
otherwise their relevance to excess mortality is not clear.

2. p4, para 1: the meta-analysis emphasised the idea of excess morbidity caused by screening not excess mortality.

3. p8, para 1: Is it the Malmo 2 study that is meant here?

Discretionary Revisions

p3, para 1: Increased incidence (ref 3) is predominantly due to screening. Therefore, I suggest adding '.. in 2005,[3] predominantly due to screening.'

p8, para 1: '.. studies, there was no ....'

p8, para 2 ' ... under 50 and 13-year ....'

p8, para 2: stats new paragraph at 'For women over 50 ... and combine with the para 3.

p8, para 2: 'The following estimates of excess mortality were obtained ...'

p9, para 1, last sentence: 'The blinded assessment of outcomes assumes equal distribution ...'

p9, para 2: I suggest altering the first sentence to 'Significant excess non-breast cancer mortality was not found, with less than a 2.5% chance of a negative screening effect of more than 4%, i.e. 13 to 29 deaths ....' and delete the last sentence of this paragraph.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I have no competing interests in my review of this article.