

## Peer Review File

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### Reviewer Comments

**Comment 1:** Lines 16&17: STAGE II is not really “early cancer”. I would suggest dividing the numbers into Stage I (which is “early”) and Stage II and higher.

**Reply 1:** Definition of ‘early-stage breast cancer’ in this manuscript was changed to include stage 0 and stage I breast cancers.

**Comment 2:** Lines 21&22 The goal of screening is to maximize detection at Stage I. Self-detection “is not necessarily associated with a late-stage disease” is not surprising. Women can feel small cancers, but “self-detection” is difficult to teach. The question is whether or not they were practicing self-examination. (BSE)  
Self-detection can, indeed, find cancers “earlier”, but the goal and success of screening is the detection of cancers that are Stage I.

**Reply 2:** Actually, 44.2% (137 out of 310) of our patients reported a history of ‘BSE’ (data not shown), however, most of the BSEs were practiced irregularly and possibly in a wrong way because some of them had their tumors identified by imaging screening though the tumors were palpable. Here we tried to emphasize that ‘self-detected breast cancer is not too late’ because up to date there are few evidence of the clinical value of BSE and thus it’s usually overlooked by physicians, not to mention by the public. Given that imaging screening of breast cancer in China has a long way to go, we believe that a proper guidance to women on BSE could help decrease detection of late-stage diseases.

**Comment 3:** Line 37 I would suggest adding:

has been [proven to save lives in Randomized, Controlled Trials (RCT) and is] widely accepted based on experiences from developed countries.

**Reply 3:** This suggestion was adopted and revision was made accordingly.

**Comment 4:** Line 41 “starts relatively late” please add at what age does “relatively late” mean.

**Reply 4:** The first nation-wide screening program in China was attempted in 2005 by the National Health and Family Planning Commission but failed due to lack of funding and concerns about false-positive results. Nevertheless, annual/biennial mammographic screening for women aged 40-69 was recommended in our 2007 national guidelines. And afterwards, several large-scale screening programs were carried out such as the 2008 Chinese National Breast Cancer Screening Program and the 2009 ‘two cancers’ screening program aiming at rural women.

**Comment 5:** Line 47 add “aimed to reveal [the] current...”

**Reply 5:** Revision was made accordingly.

**Comment 6:** Lines 88&89 Once again, I would not characterize Stage II as “early” cancers.

**Reply 6:** Definition of ‘early-stage breast cancer’ in this manuscript was changed to include stage 0- and I- breast cancers.

**Comment 7:** Lines 135-141 are problems:

“In addition, overdiagnosis has been subject to increased attention in recent years.”

In fact, “Overdiagnosis” has been “overexaggerated”.

Lines 135 &136: “Several studies showed that mortality reduction from mammographic screening was minimal but it led to substantial overdiagnosis (14, 15), which means increased detection of low-risk cancers with more favorable 138 features instead of high-risk malignancies.”.

Actually, RCT’s have shown that screening reduces deaths by 20-30% and these are underestimates due to “noncompliance” and “contamination”.

References 14 and 15 should be dropped.

Line 138: “Some argued that screening introduced lead-time bias;”

This is due to a failure to understand the fundamentals of RCT’s. RCT’s eliminate lead-time bias.

**Reply 7:** Considering the strong evidence of screening mammography in saving lives from RCTs and the overly concerned overdiagnosis based on faulty science, this paragraph was deleted and REF 14 & 15 were dropped. Besides, “underscreening” rather than “overdiagnosis” is the major concern in China today.

**Comment 8:** Lines 142 and 143: “whether there was mortality reduction largely depends on the success of the screening program (16).”

This is fairly obvious. Just running a screening program does not save lives. The imaging equipment has to be the best possible. The technologists obtaining the images need to be highly trained as do the radiologists interpreting the images.

**Reply 8:** Yes, our finding that the percentage of advanced stage (stage II-IV) cancers in screen-detected tumors was 24.9% less than that in self-detected ones also reflected the success of current screenings in real world, though mostly sporadic and opportunistic.

**Comment 9:** Line 185 “Evidence of [the] clinical value of CBE varies in studies....”

**Reply 9:** Revision was made accordingly.

**Comment 10:** Line 186 “In Canada, one study compared [the] effects of mammography combining

**Reply 10:** Revision was made accordingly.

**Comment 11:** Line 205 “Participation of [change “of” to “in”] breast cancer screening is still not satisfactory in the absence of nation-wide

**Reply 11:** Revision was made accordingly.

**Comment 12:** Most women who are not being screened find their own cancers, so these

findings are not surprising. As the authors have explained, the data on BSE are few, and not supportive, but it would be interesting to know what percentage of women found their own cancers while practicing BSE as opposed to finding it by accident.

**Reply 12:** I'm afraid that we might not be able to give an accurate answer to this question but we assume that the percentage was low. Although 137 of our patients reported a history of BSE, most of them said that they found their tumors in the bath and it was difficult to distinguish whether this examination behavior was a proper BSE or a casual check. And like I've mentioned in **reply 2**, this does not mean BSE is helpless but rather an "improper" BSE is helpless. For this, further RCTs are needed to give solid evidence.

**Comment 13:** Even though the numbers are low, it would be interesting to determine what percentage of the women having "routine" screening mammography had their cancer detected by mammography and the same for ultrasound.

**Reply 13:** 44.4% (56/126) of women who had 'routine' screening ultrasonography found their tumor by ultrasonography. And none of the 9 women who had 'routine' screening mammography identified their tumor by mammography. This is because some of them found a breast lump in the screening interval and others underwent screening ultrasonography first which identified the tumor.