Chapter 6.2

Valorization addendum
Breast cancer is the most frequently diagnosed cancer in women worldwide.\(^1\) Also in the Netherlands, breast cancer is an important threat for public health as the incidence is among the highest in Europe, and still rising.\(^2\) As in many other countries, the Netherlands has introduced a population based screening program, with the aim to find lesions for which treatment is more effective. The potential harm of breast cancer screening is the creation of unnecessary anxiety and morbidity and inappropriate economic cost.\(^3\) The Dutch screening program is funded by the national budget and therefore paid with tax revenues. In 2012 the total costs of the program were 64.6 million euro’s, which equates to 64 euro’s per screening examination. This does not include the costs of positive screening examination, which is paid by the health insurance of the recalled woman.

In this valorization paragraph we make the knowledge obtained from this thesis, available and suitable for economic and social exploitation. The findings of this thesis resulted in novel strategies to improve the efficacy of breast cancer screening program and to minimize the harms, but did not result into commercial products or new business.

In **chapter 2** we showed that, during the transition to digital screening, the availability of prior hard copy screen films for comparison would reduce the amount of repeated false positives for the same mammographic abnormality with 40%. Further, we found that patients with a repeated false positive recall for the same mammographic lesion had a significantly worse screening re-attendance (44.3%) than patients with a negative screen examination (93.2%) or a single false positive recall (65.4%).

It is important to keep the number of false positives as low as possible to avoid anxiety and psychological distress among the effected subgroup\(^4\)\(^5\)\(^7\) and to avoid unnecessary work-up costs of benign lesions. Further, the decreased re-attendance rate after a repeated false positive recall may be (partly) due to the tendency to keep women under outpatient supervision after a repeated false positive recall. Prolonged clinical surveillance of women with a previous false positive screen results in additional diagnostic and follow-up costs, compared to mammography performed within the national screening program.

To decrease the amount of distress among screened women and to avoid unnecessary work-up and surveillance costs (financed by the health insurances), we suggest that, in case a women attends digital screening for the first time after previous screen-film mammography screening, the screening radiologist should have the opportunity to compare with the previous hard copy screen-films if repeated recall is considered. This information is relevant for screening programs in other countries currently converting to digital mammography and women who have skipped the digital screening rounds following their latest SFM screen.
In chapter 3 we found that interobserver variation persisted among 26 pairs of screening radiologists at non-blinded double reading and we suggested to create specific pairs of screening radiologists to optimize screening results. Further we analyzed the breast cancers missed at screening. The analysis of individual and regional screening results, missed cancers and false positive recalls at screening mammography is an important issue of this quality assurance. A radiologist who interprets screening examinations without the opportunity to get feedback on the outcome of recalled women may be hampered to improve his/her recall behavior. This stresses the importance to monitor screening results on a local and individual scale and to provide additional training for screening radiologists with suboptimal screening results or to create specific pairs of screening radiologists. This information is relevant for screening radiologists, screening units and the Dutch Reference Centre for Cancer screening, whom is responsible for ensuring and improving the quality of the breast cancer screening program. The digitization of the screening program and the recently established linkage with the Dutch Cancer Registry database will provide more opportunities to monitor screening results on an individual basis. This further improvement of the quality control of the breast cancer screening program in the Netherlands will eventually improve the breast cancer survival and minimize the breast cancer screening harms.

In chapter 4 we determined the screening outcomes of both blinded and non-blinded double reading and we explored how to cope best with discrepant readings i.e., recall of all discrepant readings; arbitration of all discrepant readings by a third reader; arbitration of only discrepant BI-RADS 0 recalls by a third reader’. We found that blinded double reading with arbitration of discrepant BI-RADS category 0 recalls provides the optimal balance between a high screening sensitivity, relative low recall rate and relative high positive predictive value (PPV) of recall when compared to other double reading strategies.

What does this mean for the women participating in the Dutch screening program? In 2012 there were about 1 million screened women. If the screening mammograms of these women were read in a blinded fashion with arbitration of discrepant BI-RADS category 0 recalls instead of non-blinded double reading with recall of all discrepant readings (the former used reading strategy in our region), this would result in: 700 more screen-detected cancers, 400 less interval cancers and 868 less false positive screening results. This will improve breast cancer survival, as interval cancers have a worse survival, despite receiving more adjuvant chemotherapy, than screen detected cancers.8,9 The decrease in false positive screening results will reduce the amount of recalled women with anxiety and distress and reduce the work-up costs of benign lesions. An additional cost effectiveness analysis will be necessary to determine whether blinded double reading, combined with arbitration of discrepant BI-RADS 0 recalls, should become the nationwide standard in the Netherlands.
In conclusion, this thesis has a societal as well as an economic impact. It offers strategies to improve the efficacy of the breast cancers screening program by detecting more breast cancers at an early stage and thereby reduce breast cancer morbidity and mortality. Further, it offers strategies to decrease the amount of false positive screening results which will reduce the amount of women with anxiety and psychological distress, reduce unnecessary work-up costs of benign lesions, attribute to the maintenance of screening re-attendance and thereby avoid prolonged surveillance costs.
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References