Executive summary

Health Council of the Netherlands. Population Screening Act: additional MRI scan for women with high breast density. The Hague: Health Council of the Netherlands, 2011; publication no. 2011/19

This advisory report relates to an application for authorisation for a scientific study within the breast cancer population screening programme. The goal of the study is to determine whether an additional MRI scan has added value for detecting breast cancer in women with high breast density. The applicant is the Julius Center of the University Medical Center Utrecht. On 24 December 2010, the Minister of Health, Welfare and Sport asked the Health Council of the Netherlands to assess the application based on the criteria outlined in the Population Screening Act (WBO). To this end, the Council's WBO Committee examined the scientific integrity of the research proposal, accordance with legal rules for medical actions, the usefulness and risks of the study and the importance to public health.

The planned study

Women with high breast density (a relatively large amount of glandular and connective tissue) run a higher risk of breast cancer. Furthermore, tumours are more easily missed, as the tumour is less apparent on the mammogram due to the denser breast tissue. Is an additional MRI scan a solution for these women? The study selects women from the standard population screening study who have a mammogram without abnormalities and breast density greater than or equal to 75%. 7,237 women will be randomly selected and invited to undergo an additional MRI (intervention group). Four times as many women (28,948) form the

control, and will only be monitored via the cancer registry. After three rounds of screening, the drop in the number of interval tumours in the intervention group compared with the control group will be evaluated. Interval tumours are tumours discovered outside of the screening programme, this currently happens to about two in every thousand screened women in The Netherlands.

Scientific integrity

The Committee rules positively on the scientific integrity of the application. The assumption that additional MRI may have added value for women with high breast density is sufficiently scientifically substantiated. The study design is good, the required number of participants is sufficiently substantiated and the expected outcome quantifiable and testable.

Accordance with legal rules for medical actions

Recruitment and information provision to the intended participants in the study meet legally defined criteria. Although only the intervention group is informed in greater detail and asked for written consent after pre-randomisation, the reasons and substantiation for this choice are, in the opinion of the Committee, in accordance with the intent of the Population Screening Act (WBO). In ethical terms, it may be better to ask for consent prior to randomisation, as this may be seen as part of the study. By randomising first, so-called pre-randomisation, this study can avoid women with high breast density in the control group becoming worried and requesting follow-up testing on their own accord. Until such time as this study is completed and yields a positive result, such testing would be unjustified and in disagreement with the intent of the Population Screening Act (WBO). Additionally, it would make scientific assessment of the results more difficult. Pre-randomisation is admissible if three criteria are met: the study must deliver new insights, these insights must be endangered without pre-randomisation (subsidiarity) and the study must meet the proportionality requirement. According to the Committee, pre-randomisation in this study meets these criteria sufficiently. New insights are obtained and are endangered without pre-randomisation. The control group is not subjected to additional interventions and is not disadvantaged by not knowing about the study.

Usefulness and risks of the study

The Committee believes the balance of usefulness and risks to participating women is positive. The women may profit directly from the additional MRI if a tumour is found that was missed on the mammogram. If the MRI finds nothing, women will be reassured, and the risk of interval tumours may be lower. Participating women are informed sufficiently of the potential risks of the study, and enough attention is given to the discussion of false-positive results.

Importance to public health

This is a study in an identifiable high-risk group within the breast cancer population screening programme, and is therefore, in the opinion of the Committee, a serious public health problem. If the study demonstrates additional MRI has added value for these women, and cost-effectiveness analysis outcomes are positive, the study will provide means for improving breast cancer population screening. A negative study result is also valuable: this will show that additional MRI is not a useful addition to the population screening programme for these women.

Conclusion and recommendations

In the opinion of the Committee, the application meets the legal criteria outlined in the Population Screening Act (WBO). The Committee recommends that the Minister of Health, Welfare and Sport authorise this study.