Executive summary

Health Council of the Netherlands. Population screening for breast cancer: expectations and developments. The Hague: Health Council of the Netherlands, 2014; publication no. 2014/01

Randomized controlled trials, conducted in the 1970s and 1980s, have shown that mammographic screening can reduce breast cancer mortality significantly. In the period from 1989 to 1998, the Netherlands introduced a national screening programme to detect early-stage breast cancer. In 1990, the expectation was that ultimately (by around 2015) 700 fewer women in the Netherlands would die of breast cancer each year. Today, twenty-five years on, there is persistent criticism about breast cancer screening. In academic journals as well as the lay press. Therefore, the Minister of Health, Welfare and Sport wants to know how effective population screening for breast cancer in the Netherlands really is.

The usefulness of breast cancer screening

The Minister's question is not an easy one to answer. The sheer complexity of population screening makes it very difficult to evaluate this activity. An accurate estimate of a programme's benefits and harms can be obtained only after a sufficient follow-up. In addition, population screening for breast cancer was introduced at a time of radical change in the treatment of breast cancer. Since then, the treatment of breast cancer has greatly improved, and is still undergoing rapid development. Moreover, women have become more aware of breast cancer, and are quicker to consult their GP than were their predecessors. The situation today is very different from what it was 25 years ago.

The breast screening debate has not helped to have a clear view of the usefulness of mammographic screening. Some researchers argue that the benefit of screening is overstated and that the overdiagnosis associated with screening is understated. They are not convinced that what (in their view) is a very marginal benefit, really compensates for the drawbacks involved in such programmes. Other researchers believe that population screening actually yields important health gains. The findings vary widely. Why is this? According to the Committee, the explanation lies primarily in the area of research methodology.

Benefits of population screening

Given the continuing controversy about the effectiveness of breast cancer screening, the Committee has delved even more deeply than usual into the methodology of various types of evaluation study. It concluded that it is generally not possible to draw any hard and fast conclusions from trend studies. Screening effects can, however, be measured by means of well-designed cohort studies and case-control studies. This approach makes it possible to distinguish a screening effect from other factors that affect breast cancer mortality, such as improved treatment.

Based on evidence from the most reliable cohort studies, a breast cancer mortality reduction of 26 percent can be expected from service screening offered (but not all of whom participated) to women aged 50-69. Case-control studies determine the relationship between actual participation in screening and breast cancer mortality. The results consistently show that participation in screening is associated with a significant reduction in breast cancer mortality.

In the Netherlands from 1986/1988 breast cancer mortality (European standardized rate) declined by 34 percent to 62 per 100.000 women 50 to 75 years of age in 2012. It is difficult to determine exactly how much of this 34 percent decline is attributable to population screening. Based on computer modeling, it is estimated that about half of this decline is due to population screening, and the remainder to improved treatment.

The conclusion is that the effectiveness of population screening for breast cancer in the Netherlands continues to meet the initial expectations, even though circumstances have changed greatly over the intervening years. This leads to the question of whether the benefits of such population screening outweigh the ever-present drawbacks involved in this exercise.

Harms of population screening

Population screening also has a number of drawbacks. To obtain a good-quality mammogram, the breast must be firmly compressed. Half of the participants find this experience unpleasant or even painful. For every thousand participants, there are seventeen false alarms (false positives), i.e. women who are told that they may have breast cancer, while this later turns out not to be the case. It can also happen that screening enables cases of breast cancer to be diagnosed that would never have been identified clinically in the lifetime of a woman if screening had not been carried out ("overdiagnosis"). In any given individual case, it is impossible to know whether or not overdiagnosis is involved. So treatment is routinely given. As a result, a part of the women in question experience all of the drawbacks but none of the benefits of early diagnosis and treatment.

The frequency of overdiagnosis can only be estimated at population level over a period of several years. The estimated percentages vary considerably, ranging from 0 percent to more than half of all cases of breast cancer diagnosed among women in the screening age-range. This has, quite naturally, generated a great deal of debate. The use of different definitions gives rise to confusion. Another important factor is the length of the observation period. This is because screening allows diagnoses to be made two to three years earlier (the "lead time"), on average. As a result, cases of breast cancer are diagnosed more frequently than usual during the introductory stage of a population screening programme (the "prevalence peak"). Conversely, when women have reached the age of 75 and no longer undergo screening, fewer cases of breast cancer are diagnosed than is usual for women of that age. This compensatory drop in incidence can fully be estimated observed only if all women in the age group above the screening age have been invited to screening when they were in the eligible age range.

This means that the level of overdiagnosis can only be estimated after a long period of follow-up. Researchers who only take the introductory stage into consideration, without allowing for the subsequent compensatory drop or without correcting for lead time, overestimate the level of overdiagnosis. Adequate studies tend to produce significantly lower figures, ranging from one to ten percent overdiagnosis relative to the expected incidence of breast cancer in the absence of screening. At three percent, the estimate for the Netherlands falls within this range. This corresponds with the value of eight percent for screen detected cases of breast cancer. The conclusion is that overdiagnosis does indeed occur, but not to the extent that is often suggested.

Risk-benefit ratio

How do the benefits of the Netherlands' current screening programmes weigh up against the drawbacks involved? Cost-effectiveness analuysis shows that screening avoids on average 775 deaths from breast cancer on a yearly base, and that 1,200 women would need to be screened to prevent one death from breast cancer. For each prevented death from breast cancer, 23 women will be referred every year. Of these, 16 will be found to have a false positive screening result. Of each seven to eight true positive results, 5 involve no health gains at all (with the possible exception of less invasive treatment as a result of early diagnosis). Of 0.9 woman of these true positives will die from breast cancer despite having participated in the screening programme, and without screening 0.5 individuals in that group would never have had to face a diagnosis of "breast cancer".

Cost-effectiveness analysis shows that the costs of population screening programmes in the Netherlands amount to EUR 1,600 per year of life gained. For each death from breast cancer prevented by screening, aside from being spared the terminal stages of this disease, the woman in question will gain an average of 16.5 years of life.

The statement that screening generates more overdiagnosis than health benefits does not apply to population screening in the Netherlands. On scientific grounds, there are no compelling reasons to terminate this screening programme.

Modifications to the current screening programme

The Minister asked what modifications and changes might be needed to further improve this population screening programme. As e first step, an alternative referral pathway is developed for women with BI-RADS 0 screening results. In such cases, there is only a small risk of breast cancer. For 60 percent of the participants with BI-RADS 0, the use of imaging techniques (mammagraphy and ultrasound) is sufficient to exclude a diagnosis of "breast cancer", without the need for invasive diagnostic tests. Fast-tracking individuals to diagnostic imaging would help to alleviate much of the fear and anxiety caused by the screening result.

It has been found that, even after being given a diagnosis of "benign breast abnormality", women with false positive screening results nevertheless often undergo further outpatient check-ups. Is this because they remain insecure and fearful? In which case, is the offer of a follow-up appointment an adequate response? Or might this be a job for the GP? Further research could highlight ways of improving the guidance offered to such women.

A number of studies are currently under way in the Netherlands into topics such as the compression plates used in mammography to compress the breast; the use of a special film on the compression plate and the bucky to enable more breast tissue to be imaged; and a new, pressure-guided compression method. In the short term, these studies may identify ways of making mammography less painful, without impairing the quality of the mammogram or affecting the radiation dose.

According to the Committee, there are no compelling scientific reasons for modifying either the target group's age limits, the screening interval, or the screening method.

Developments with potential promise in the medium-term

Population screening currently offers the same screening programme to all women in the target group. One appealing way of improving the risk-benefit ratio of screening would be to adapt this process to the individual risk of breast cancer involved. Using existing risk models, however, it is not possible to draw sharp distinctions on the basis of risk. Better risk assessment will probably be possible when more comprehensive models become available. Risk factors such as mammographic breast-tissue density and blood tests for genetic variants and sex hormones, in particular, may have added value. A great deal of research is currently focusing on candidate markers and the validity of new risk models. There are also questions regarding the logistics of risk stratification in the context of service screening, and the effects of providing intensive screening (younger starting age, additional screening method) to the high-risk group and less intensive screening to the low-risk group.

A new technique, tomosynthesis, can supplement regular two-dimensional mammograms by constructing three-dimensional images of the breast. Tomosynthesis offers great promise, as a method for improving cancer detection and reduce the number of false positives. As yet, its drawbacks are higher radiation exposure, longer exposure time (so the pain also lasts longer), and longer interpretation time. A number of major issues remain to be resolved before trial population screening to assess this technique can be contemplated.

Conclusion

The Committee concludes that population screening is still worthwhile. Each year, it prevents on average 775 deaths from breast cancer. The main disadvantage of screening will occur in about 8 percent of screen detected cases.

A substantial disadvantage, but not to the extent that is often suggested. Dutch population screening stands out in terms of its high participation rate and low referral rate combined with reliable test performance. Further improvements are expected in the near future, involving new techniques that make the procedure less painful and that reduce the radiation dose involved in mammographic screening (which is already low) by half. In the longer term, it may be possible to design more efficient population screening programmes. For instance, rather than submitting all women to the same screening procedure, a range of options could be developed, each tailored to an individual's estimated risk of breast cancer.