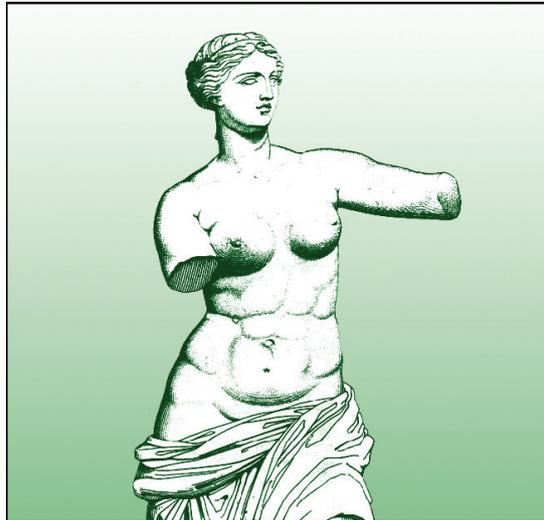


SCREENING FOR BREAST CANCER WITH MAMMOGRAPHY



What are the benefits and harms of attending a screening programme?

How many will benefit from being screened, and how many will be harmed?

What is the scientific evidence for this?

Contents

Summary	3
Why have we written this leaflet?	4
What is screening?	4
Benefits	5
Harms	5
Documentation for our facts and figures.....	7
References	10

Written by:

Peter C. Gøtzsche, chief physician, DrMedSci, director, The Nordic Cochrane Centre, Rigshospitalet, Copenhagen, Denmark.

Ole J. Hartling, chief physician, DrMedSci, chairman, The Ethical Council, Denmark.

Margrethe Nielsen, midwife, MSc, Danish Consumer Council.

John Brodersen, general practitioner, PhD, University of Copenhagen, Denmark.

This leaflet is available at: www.screening.dk and www.cochrane.dk.

January, 2008

Summary

It may be reasonable to attend for breast cancer screening with mammography, but it may also be reasonable not to attend, as screening has both benefits and harms.

If 2000 women are screened regularly for 10 years, one will benefit from the screening, as she will avoid dying from breast cancer.

At the same time, 10 healthy women will, as a consequence, become cancer patients and will be treated unnecessarily. These women will have either a part of their breast or the whole breast removed, and they will often receive radiotherapy, and sometimes chemotherapy.

Furthermore, about 200 healthy women will experience a false alarm. The psychological strain until one knows whether or not it was cancer, and even afterwards, can be severe.

Why have we written this leaflet?

We have written this leaflet because the information women receive, when they are invited to attend for screening with mammography, is insufficient and one-sided. The letters of invitation emphasize the benefits of screening, but they do not describe how many healthy women will experience the most important harms, overdiagnosis and overtreatment.

When women are invited to screening, the practice often is that, when they receive a letter about mammography screening, they are also given an appointment time for the examination. This procedure puts pressure on women to attend. Because of this, their participation becomes less voluntary.

Women who seek additional information on web sites on the internet are also badly served, as the most important harms are usually not mentioned at all. There are a few exceptions, however, e.g. the National Breast Cancer Coalition (www.stopbreastcancer.org), whose members are mainly women with breast cancer, and the Center for Medical Consumers (www.medicalconsumers.org), both from the USA.

We hope this pamphlet gives sufficient information about the benefits and harms of screening with mammography to enable a woman - together with her family and her doctor - to make a decision on an informed basis whether or not to attend for screening.

The pamphlet is available at www.screening.dk and www.cochrane.dk. We welcome proposals and criticism, at general@cochrane.dk.

What is screening?

Screening means to examine a population group in order to detect disease.

In several countries, women between 50 and 69 years of age are offered an X-ray examination of the breasts – screening with mammography - every second or third year. The purpose of the

examination is to find women who have breast cancer in order to offer them earlier treatment.

Screening with mammography has both benefits and harms, and it should be up to the individual woman to weigh the pros and cons. It may be reasonable to attend screening, but it may be equally reasonable not to attend. The examination is not a duty, but an offer that the woman may or may not wish to accept.

It is often claimed that if nothing abnormal is found by screening, it makes the woman feel reassured that she is healthy. But almost all women will feel healthy before they are invited to screening, and the invitation may also cause insecurity. Therefore, one cannot say that screening leads to reassurance. It creates both security and insecurity.

Benefits

Better survival - Regular screening with mammography cannot prevent breast cancer, but it can reduce the risk of dying from breast cancer.

If 2000 women are screened regularly for 10 years, one will benefit from screening, as she will avoid dying from breast cancer because the screening detected the cancer early.

Harms

Overdiagnosis and overtreatment - Some of the cancerous tumours and so-called precursors of cancer that are found by screening grow very slowly, or not at all ("pseudo-cancers"). They would therefore never have developed into a real cancer. Since it is not possible to tell the difference between the dangerous and the harmless cell changes, all of them are treated. Screening therefore results in treatment of many women for a cancer disease they do not have, and that they will not get.

If 2000 women are screened regularly for 10 years, 10 healthy women will be turned into cancer patients and will be treated unnecessarily. These women will have either a part

of their breast or the whole breast removed, and they will often receive radiotherapy, and sometimes chemotherapy.

Unfortunately, some of the very early cell changes (which, in medical language, are called carcinoma in situ) are often found in several places in the breast. Therefore, the whole breast is removed in one out of four of these cases, although only a minority of the cell changes would have developed into cancer.

More extensive surgery and aftertreatment - For some women, the operation and aftertreatment may be less extensive when a small "true" cancer was detected by screening, than if it was detected at a later time. However, as screening leads to overdiagnosis and overtreatment of healthy women, more women will lose their breast when there is screening than if there had not been screening. Also, more women will receive radiotherapy.

False alarm - If the X-ray shows something that might be cancer, the woman is recalled for additional investigations. In some cases it turns out that what was seen on the X-ray was benign, and that it was therefore a false alarm.

If 2000 women are screened regularly for 10 years, about 200 healthy women will experience a false alarm. The psychological strain until it is known whether or not there is a cancer, can be severe. Many women experience anxiety, worry, despondency, sleeping problems, changes in the relationships with family, friends and acquaintances, and a change in sex drive. This can go on for months, and in the long term some women will feel more vulnerable about disease and will see a doctor more often.

Pain at the examination - The breast is squeezed flat between two plates while an X-ray is taken. It only takes a moment, but about half of the women find it painful.

False reassurance - Not all cancers can be detected by X-ray. It is therefore important that the woman sees a doctor if she finds a lump in her breast, even if she has had a mammogram recently.

Documentation for our facts and figures

The information we have given in this pamphlet is different from the information found in most other materials, e.g. in invitations for screening (1) or from cancer charities and other interest groups (2). We therefore provide the background for our numbers below and explain why other numbers about screening are not equally reliable.

The most reliable results come from trials where the women have been randomized to be screened or not to be screened. About half a million healthy women have participated in such trials (3). Most randomized trials have been carried out in Sweden. A review of the Swedish trials from 1993 showed that screening reduced breast cancer mortality by 29% (4). The review also noted that after 10 years of screening, this reduction in mortality corresponded to saving one woman out of 1000. The benefit of screening is thus very small. The reason for this is that in a period of 10 years only 3 women out of 1000 get breast cancer and die from it. The real reduction in mortality was therefore only 0.1% (1 out of 1000) after 10 years in the Swedish trials. However, in a review of the Swedish trials from 2002, the reduction in mortality was only 15% with one method of calculation, and 20% with another method (5). The two reviews of the Swedish trials have the shortcoming that the researchers did not take into account that some of the trials had been better done - and therefore are more reliable - than others.

The most thorough evaluation of all the randomized trials that exists is a Cochrane review (3). Here, the mortality reduction was 7% in the best trials and 25% in the poorest, and since poor trials usually overestimate the effect, the mortality reduction was estimated to be 15% (3). Another thorough evaluation of the trials has been carried out on behalf of the U.S. Preventive Services Task Force. The researchers found an effect of 16% (6). Hence, these two systematic reviews found an effect on breast cancer mortality that was only half as large as in the first Swedish review from 1993. This means that regular screening of 2000 women for 10 years is necessary to save one of them from dying of breast cancer, i.e. an effect of 0.05%.

An effect of screening on mortality from all causes has not been demonstrated. Thus, it has not been shown that women who attend screening live longer than women who do not attend screening.

The randomized trials showed that screening increased by 30% the number of women who got a breast cancer diagnosis and were treated, compared with the group that was not screened (3). Large population studies from the Nordic countries, United Kingdom, USA and Australia have confirmed that screening results in an overdiagnosis of 30-40% (3,7). The randomized trial that followed the participants the longest showed a 25% rate of overdiagnosis in the mammography-screened women (8) (this calculation took into account the fact that many women in the control group had mammograms, though they had not been invited to be screened).

From the Cochrane review (3) it can be calculated what an overdiagnosis of 30% means for the women. In the trials from Canada and Malmö, either the whole breast or part of it was removed in 1424 women in the screened group and in 1083 women in the control group. Since the control group comprised 66,154 women, the overdiagnosis constituted $(1424-1083)/66,154 \times 2000 = 10$ women per 2000 screened women. Thus, by screening 2000 women, 10 healthy women will get a cancer diagnosis they would not have had if they had not been screened, and they are also treated as if they were cancer patients.

A study of screening for breast cancer in Denmark concluded that it is possible to screen without overdiagnosis (9). However, the study provided no justification for this statement. In another study, co-authored by some of the same investigators, it can be calculated that the number of breast cancer diagnoses increased markedly in Copenhagen after screening was introduced (10). According to data from the National Board of Health on the number of breast cancer diagnoses, screening in Denmark results in substantial overdiagnosis.

The Cochrane review showed that the breast was removed in 20% more women in the screened group than in the control group (3). Other studies have also shown that more breasts are removed when there is screening than when there is no screening (3). Furthermore, in the United Kingdom the whole breast was removed in 29% of those cases where the cancerous lesions were

detected in very early stages when they had not spread, although those should have been the very cases where a less extensive operation could have been performed (11).

The psychological strain until it is known whether or not there is a cancer, can be severe (3, 12). In the USA it has been calculated that after 10 rounds of screening, 49% of healthy women will have experienced a false alarm (13). In Norway, 21% will have experienced a false alarm after 10 rounds of screening (14). However, the numbers for Norway and most other countries are too low because recalls due to poor technical quality of the mammogram have usually not been included (14). As the women are just as affected by such recalls as by a real suspicion of cancer (12), they should be counted as false alarms. In Copenhagen, 6% of the women experienced a false alarm at the first screening round (15), and 10% of the women who had turned up for the first 3 rounds experienced a false alarm (16). The researchers have estimated that 10% will have experienced a false alarm in Denmark after 10 years of screening (5 rounds), which corresponds to 200 healthy women for each 2000 women screened regularly for 10 years. This estimate may be a bit too low, however.

We have mentioned earlier that about half of the women experience pain at mammography when the breasts are squeezed flat. This appears from a systematic review of the relevant studies (17).

References

1. Jørgensen KJ, Gøtzsche PC. Content of invitations to publicly funded screening mammography. *British Medical Journal* 2006; 332:538-41.
2. Jørgensen KJ, Gøtzsche PC. Presentation on websites of possible benefits and harms from screening for breast cancer: cross sectional study. *British Medical Journal* 2004; 328:148-51.
3. Gøtzsche PC, Nielsen M. Screening for breast cancer with mammography. *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD001877 (kan også læses på www.cochrane.dk).
4. Nyström L, Rutqvist LE, Wall S, Lindgren A, Lindqvist M, Ryden S, et al. Breast cancer screening with mammography: overview of Swedish randomised trials. *Lancet* 1993; 341:973-8.
5. Nyström L, Andersson I, Bjurstam N, Frisell J, Nordenskjöld B, Rutqvist LE. Long-term effects of mammography screening: updated overview of the Swedish randomised trials. *Lancet* 2002; 359:909-19.
6. Humphrey LL, Helfand M, Chan BK, Woolf SH. Breast cancer screening: a summary of the evidence for the U.S. Preventive Services Task Force. *Annals of Internal Medicine* 2002; 137(5 Part 1):347-60.
7. Giles GG, Amos A. Evaluation of the organised mammographic screening programme in Australia. *Annals of Oncology* 2003; 14:1209-11.
8. Gøtzsche PC, Jørgensen KJ. Estimate of harm/benefit ratio of mammography screening was five times too optimistic. <http://bmj.bmjournals.com/cgi/eletters/332/7543/691>, 2006.
9. Olsen AH, Jensen A, Njor SH, Villadsen E, Schwartz W, Vejborg I, Lynge E. Breast cancer incidence after the start of mammography screening in Denmark. *British Journal of Cancer* 2003; 88:362-5.
10. Törnberg S, Kemetli L, Lynge E, Olsen AH, Hofvind S, Wang H, Anttila A, Hakama M, Nyström L. Breast cancer incidence and mortality in the Nordic capitals, 1970-1998. Trends related to mammography screening programmes. *Acta Oncologica* 2006; 45:528-5.
11. NHS cancer screening programmes. BASO Breast Audit 1999/2000. www.cancerscreening.nhs.uk/breastscreen/publications.html (accessed Dec 12, 2001).
12. Brodersen J. Measuring psychosocial consequences of false-positive screening results - breast cancer as an example (ph.d.-afhandling). Department of General Practice, Institute of Public Health, Faculty of Health

Sciences, University of Copenhagen. Månedsskrift for Praktisk Lægegering 2006 (ISBN 87-88638-36-7).

13. Elmore JG, BartonMB, Mocer VM, Polk S, Arena PJ, Fletcher SW. Ten-year risk of false positive screening mammograms and clinical breast examinations. The New England Journal of Medicine 1998; 338:1089–96.

14. Hofvind S, Thoresen S, Tretli S. The cumulative risk of a false-positive recall in the Norwegian Breast Cancer Screening Program. Cancer 2004; 101:1501-7.

15. Vejborg I, Olsen AH, Jensen MB, Rank F, Tange UB, Lynge E. Early outcome of mammography screening in Copenhagen 1991-99. Journal of Medical Screening 2002; 9:115-9.

16. Lynge E. Mammography screening for breast cancer in Copenhagen April 1991-March 1997. Mammography Screening Evaluation Group. APMIS-Suppl 1998; 83:1-44.

17. Armstrong K, Moyer E, Williams S, Berlin JA, Reynolds EE. Screening mammography in women 40 to 49 years of age: a systematic review for the American College of Physicians. Annals of Internal Medicine 2007; 146:516-26.

Other relevant literature

Welch H. Should I be tested for cancer? Maybe not and here's why. Berkeley: University of California Press; 2004.

Vainio H, Bianchini F. IARC Handbooks of Cancer Prevention. Vol 7: Breast Cancer Screening. Lyon: IARC Press, 2002 (written by a working group under WHO).

Further information can be obtained by contacting the doctor