

EDITORIALS

Too much mammography

Long term follow-up does not support screening women under 60

Mette Kalager *medical doctor and researcher*^{1,2,3}, Hans-Olov Adami *professor*^{1,2,4}, Michael Bretthauer *professor*^{1,2,5,6}

¹Department of Health Management and Health Economics, University of Oslo, Oslo, Norway; ²Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA; ³Department of Research and Development, Telemark Hospital, Skien, Norway; ⁴Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; ⁵Department of Transplantation Medicine, Oslo University Hospital, Oslo, Norway; ⁶Department of Medicine, Sørlandet Hospital Kristiansand, Kristiansand, Norway

Before being widely implemented, mammography screening was tested in randomised controlled trials in the 1960s to 80s. Meta-analyses of these trials showed a relative reduction in deaths from breast cancer of between 15% and 25% among women aged 50 to 69.¹⁻³ Only the Canadian National Breast Screening Study showed no reduction in breast cancer mortality.¹⁻³ This large randomised controlled trial compared physical breast examination with combined physical breast examination and annual mammography in women aged 40 to 59.¹⁻³

In a linked paper (doi:10.1136/bmj.g366), Miller and colleagues present the results for up to 25 years of follow-up in the Canadian study.⁴ No difference in breast cancer mortality was observed between the mammography and control arms, whereas a significant excess incidence of invasive breast cancer was observed in the mammography arm, resulting in 22% overdiagnosis. This means that 22% of screen detected invasive cancers would not have reduced a woman's life expectancy if left undetected.

The major strengths of this study include its randomised design, intense intervention with five annual mammography screenings, high compliance, and complete, long term follow-up. The lack of mortality benefit is also biologically plausible because the mean tumour size was 19 mm in the screening group and 21 mm in the control group. This 2 mm difference—which might be even smaller if overdiagnosed cancers could be excluded from the screening group—represents a minimal proportion of the entire clinical course for breast tumours.

But the trial also has some potential limitations. No quantitative data are available on the degree of contamination in the control arm or possible confounding by screening mammography after the trial. It seems unlikely, however, that such potential limitations would conceal a clinically important benefit. The

rate of overdiagnosis did not include ductal carcinoma in situ, and the trial provides no data for women older than 60.

The Canadian study, launched in 1980, is the only trial to enroll participants in the modern era of routine adjuvant systemic treatment for breast cancer, and the women were educated in physical breast examination as advocated today.⁴ These important features may make this study more informative for a modern setting, compared with other randomised trials. The results of the study are strikingly similar—for both lack of efficacy and extent of overdiagnosis—to recent studies evaluating today's screening programmes.⁵⁻⁷ The real amount of overdiagnosis in current screening programmes might be even higher than that reported in the Canadian study,⁴ because ductal carcinoma in situ, which accounts for one in four breast cancers detected in screening programmes,⁸ was not included in the analyses.

Other studies also indicate that improved treatment rather than screening is the reason for the decline in breast cancer mortality during the past four or five years.^{5,7} Even though different studies arrive at different reductions in breast cancer mortality (from 10% to 25%), these benefits translate to only marginal differences in absolute effects. Much larger variation is seen in the estimates of overdiagnosis.⁶ In studies based on statistical modelling, overdiagnosis was less than 5%.⁶ By contrast, most observational studies report higher estimates of overdiagnosis, ranging from 22% to 54%,⁶ depending on denominator used.⁹ When the number of breast cancers detected at screening is used as the denominator (as in the Canadian study), the amount of overdiagnosis observed in the previous randomised controlled trials is strikingly similar (22-24%).^{4,10}

How do the data on mammography screening compare with data on prostate cancer screening by prostate specific antigen, which is currently not encouraged in the United Kingdom and other countries owing to its small effect on mortality and large

Correspondence to: M Kalager mette.kalager@medisin.uio.no

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Figure showing 20 year risk for diagnosis of, and death from, breast and prostate cancer with and without screening in the United Kingdom

risk of overdiagnosis (www.screening.nhs.uk/prostatecancer)? The figure on bmj.com shows that the absolute harms (overdiagnosis) and benefits (mortality reduction) are not very different between the screening types. The 20 year risk of breast cancer for a 50 year old woman is 6.1% with screening (including 22% overdiagnosis⁴),¹¹ and 5.0% without screening; and the corresponding numbers for prostate cancer in a 50 year old man are 3.9% with screening (including 45% overdiagnosis¹²) and 2.7% without screening.¹¹ The 20 year risk of death from cancer for a 55 year old woman is 1.5% with screening (assuming a 20% reduction in mortality²)¹¹ and 1.9% without screening; and the corresponding numbers for prostate cancer in a 55 year old man are 1.0% with (assuming a 20% reduction in mortality¹²) and 1.3% without screening.¹¹

Nevertheless, the UK National Screening Committee does recommend mammography screening for breast cancer but not prostate specific antigen screening for prostate cancer, stating that the “aim is to only implement programs that do more good than harm and that the informed choice is a guided principle of screening” (www.screening.nhs.uk/screening). Because the scientific rationale to recommend screening or not does not differ noticeably between breast and prostate cancer, political pressure and beliefs might have a role.

We agree with Miller and colleagues that “the rationale for screening by mammography be urgently reassessed by policy makers.” As time goes by we do indeed need more efficient mechanisms to reconsider priorities and recommendations for mammography screening and other medical interventions. This is not an easy task, because governments, research funders, scientists, and medical practitioners may have vested interests in continuing activities that are well established.

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- 1 Gotzsche P, Jørgensen KJ. Screening for breast cancer with mammography. *Cochrane Database Syst Rev* 2013;6:CD001877.
- 2 The Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. 2012. www.cancerresearchuk.org/sites/default/files/breast-screening-review-exec_0.pdf.
- 3 Vainio H, Bianchini F, eds. IARC handbook of cancer prevention. Vol 7. Breast cancer screening. IARC Press, 2002.
- 4 Miller AB, Wall C, Baines CJ, Sun P, To T, Narod SA. Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. *BMJ* 2014;348:g366.
- 5 Kalager M, Zelen M, Langmark F, Adami HO. Effect of screening mammography on breast-cancer mortality in Norway. *N Engl J Med* 2010;363:1203-10.
- 6 Kalager M, Adami H-O, Bretthauer M, Tamimi RM. Overdiagnosis of invasive breast cancer due to mammography screening: results from the Norwegian Screening Program. *Ann Intern Med* 2012;156:491-9.
- 7 Autier P, Boniol M, Gavin A, Vatten L. Breast cancer mortality in neighbouring European countries with different levels of screening but similar access to treatment: trend analysis of WHO mortality database. *BMJ* 2011;343:d4411.
- 8 Bundred N, Dixon MJ. Carcinoma in situ. *BMJ* 2013;347:f3289.
- 9 Kalager M, Løberg M, Fønnebo VM, Bretthauer M. Failure to account for selection-bias. *Int J Cancer* 2013;133:2751-3.
- 10 Welch HG, Schwartz LM, Woloshin S. Ramifications of screening for breast cancer: 1 in 4 cancers detected by mammography are pseudocancers. *BMJ* 2006;332:727.1.
- 11 Steliarova-Foucher E, O'Callaghan M, Ferlay J, Masuyer E, Forman D, Comber H, et al. European Cancer Observatory: cancer incidence, mortality, prevalence and survival in Europe. Version 1.0 (September 2012). European Network of Cancer Registries, International Agency for Research on Cancer. <http://eco.iarc.fr>.
- 12 UK National Screening Committee. Option appraisal: screening for prostate cancer. Update March 2013. www.screening.nhs.uk/prostatecancer.

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