

cancers in the study group contemporaneously with the control group's closure screen somehow invalidates the design and analysis. The PSP screen is a prevalent screen, whereas at that time, the ASP is in incident screen mode. The appropriate comparison is with the prevalent screen of the ASP, which was published in 1992 and shows similar results to the PSP closure screen.⁴

The criticism of the Swedish Two-County Trial on the grounds of imbalances in missing values is inaccurate, not only are we unable to verify these figures from the trial data, we cannot find them in the paper that Autier et al cite as the source.⁴

The issue of potential bias in cause of death has been examined time and again and shown to be a red herring.⁵⁻⁷ Indeed, the Swedish overview has published the excess mortality analysis which does not require classification of cause of death and found essentially the same mortality reduction as in the cause-specific analysis.⁸

The paper does not contribute to the debate on the value of mammographic screening, but confuses the discussion due to fatal errors that negate their conclusions.

Declarations

Competing interests: None declared

References

1. Autier P, Boniol M, Smans M, Sullivan R and Boyle P. Statistical analyses in Swedish randomised trials on mammography screening and in other randomised trials in cancer screening: a systematic review. *J R Soc Med* 2015; DOI: 10.1177/0141076815593403).
2. Duffy SW and Smith RA. A note on the design of cancer screening trials. *J Med Screen* 2015; 22: 65–68.
3. Tabar L, Fagerberg CJG, Gad A, et al. Reduction in mortality from breast cancer after mass screening with mammography: Randomised trial from the Breast Cancer Screening Working Group of the Swedish National Board of Health and Welfare. *Lancet* 1985; i: 829–832.
4. Tabar L, Fagerberg G, Duffy SW, Day NE, Gad A and Grontoft O. Update of the Swedish two-county program of mammographic screening for breast cancer. *Radiol Clin Nth Amer* 1992; 30: 187–210.
5. Tabar L, Fagerberg G, Duffy SW and Day NE. The Swedish two-county trial of mammographic screening for breast cancer: Recent results and calculation of benefit. *J Epidemiol Comm Hlth* 1989; 43: 107–114.
6. Tabar L, Duffy SW, Yen MF, Warwick J, Vitak B, Chen HHT and Smith RA. All-cause mortality among breast cancer patients in a screening trial: support for breast cancer mortality as an endpoint. *J Med Screening* 2002; 9: 159–162.
7. Holmberg L, Duffy SW, Yen AMF, Tabar L, Vitak B, Nyström L and Frisell J. Differences in endpoints between the Swedish W-E (two-county) trial of mammographic screening and the Swedish overview: methodological consequences. *J Med Screening* 2009; 16: 73–80.
8. Larsson LG, Nyström L, Wall S, et al. The Swedish randomised mammography screening trials: analysis of their effect on the breast cancer related excess mortality. *J Med Screen* 1996; 3: 129–132.

László Tabar

Falun Central Hospital, Falun, Sweden
Email: laszlo@mammographyed.com

Nicholas Day

University of Cambridge, Cambridge, UK,

Robert Smith

American Cancer Society, Atlanta, USA,

Tony HH Chen

National Taiwan University, Taipei, Taiwan,

Amy MF Yen

Taipei Medical University, Taipei, Taiwan

Stephen Duffy

Queen Mary University of London, London, UK

for the Swedish Two-County Research Group

Screening mammography: Authors' response to Nyström and Tabar and colleagues

The correspondence of Tabar et al. and of Nyström essentially attempt to justify their statistical approach. Notably, no evidence is cited which is not linked to the Swedish trials, the focus of our comments. Two co-authors recently attempted to justify the incorporation approach using complex mathematical arguments.¹ The incorporation approach was used for the first time in 1992,² and it is surprising that it took so long to see a more formal explanation. The conduct and reporting of intervention studies in humans should be based on transparent methods validated by the scientific community at large. In this regard, a single publication in which it is necessary to have recourse to complicated mathematical arguments for substantiating the incorporation approach underlines the precariousness of this approach.

Tabar et al. evoke a lead time effect by which the screen detection of some cancers during the intervention period would have prevented the occurrence of

clinical cancers during the post-intervention period. It would then be expected that the incidence of cancers in the screening group should decline at least transiently after termination of the intervention. However, the Goteborg trial showed that there was no slowing down of incidence trends in years following the intervention period.³

The initial publication of the two-county trial reported a 31% reduction in breast cancer mortality.⁴ However, all further reports on this trial had recourse to the incorporation method for keeping the reduction at 31%. Surprisingly, overviews that also used the incorporation approach reported mortality reductions of 22% or less for this trial.^{5,6} The 9% difference thus reflects the underreporting of breast cancer as the underlying cause of death in the screening group. If, in addition, the effect of incorporation approach was removed in a way similar to what we did in our article, then breast cancer mortality reductions would be in the order of 13% or less.

Nyström evokes notoriety and authority arguments that have no place in contemporary scientific discussions. Nyström states that Swedish trials on mammography screening did not differ from large clinical trials. This is incorrect. Trials based on the left-to-nature design cannot implement blinding procedures of subjects and of health professionals that are typical of trials testing the efficacy of drugs. This limitation paves the way to cause of death misclassification and to biases due to differences in disease awareness and in patient management between randomisation groups.

We have acknowledged Nyström's efforts for examining correlations between causes of death until 31 December 1989 reported on death certificates and by health professionals not involved in mammography trials. However, after 1989, causes of death were based on death certificates only, and it is totally unknown whether the correlation maintained until 31 December 1996, when there were about two times more deaths than on 31 December 1989. Of note, a German study on screening for cutaneous melanoma illustrates well the untoward consequences of the absence of blinding on the way doctors complete death certificates.⁷

This important debate demands wider scientific scrutiny.

Declarations

Competing interests: None declared

References

1. Duffy SW and Smith RA. A note on the design of cancer screening trials. *J Med Screen* 2015; 22: 65–68.

2. Tabar L, Fagerberg G, Duffy SW, Day NE, Gad A and Grontoft O. Update of the Swedish two-county program of mammographic screening for breast cancer. *Radiol Clin North Am* 1992; 30: 187–210.
3. Bjurstam N, Bjorneld L, Warwick J, et al. The Gothenburg breast screening trial. *Cancer* 2003; 97: 2387–2396.
4. Tabar L, Fagerberg CJ, Gad A, et al. Reduction in mortality from breast cancer after mass screening with mammography. Randomised trial from the Breast Cancer Screening Working Group of the Swedish National Board of Health and Welfare. *Lancet* 1985; 1: 829–832.
5. Nyström L. Breast cancer screening with mammography: overview of Swedish randomised trials. *Lancet* 1993; 341: 973–978.
6. Nyström L, Andersson I, Bjurstam N, Frisell J, Nordenskjöld B and Rutqvist LE. Long-term effects of mammography screening: updated overview of the Swedish randomised trials. *Lancet* 2002; 359: 909–919.
7. Stang A and Jöckel KH. Does skin cancer screening save lives? A detailed analysis of mortality time trends in Schleswig-Holstein and Germany. *Cancer* 2015; doi: 10.1002/cncr.29755. [Epub ahead of print].

Philippe Autier

University of Strathclyde Institute of Global Public Health, International Prevention Research Institute, Espace Européen, Building G, Allée Claude Debussy, Ecully, Lyon 69130, France
International Prevention Research Institute, 95 Cours Lafayette, Lyon 69006, France
Email: philippe.autier@i-pri.org

Mathieu Boniol

University of Strathclyde Institute of Global Public Health, International Prevention Research Institute, Espace Européen, Building G, Allée Claude Debussy, Ecully, Lyon 69130, France
International Prevention Research Institute, 95 Cours Lafayette, Lyon 69006, France

Michel Smans

International Prevention Research Institute, 95 Cours Lafayette, Lyon 69006, France

Richard Sullivan

Institute of Cancer Policy, Kings Health Partners Cancer Centre, Guy's Campus, London SE1 9RT, UK

Peter Boyle

University of Strathclyde Institute of Global Public Health, International Prevention Research Institute, Espace Européen, Building G, Allée Claude Debussy, Ecully, Lyon 69130, France
International Prevention Research Institute, 95 Cours Lafayette, Lyon 69006, France