

Dear Editor,

In their recent article, Jørgensen and colleagues compare changes over time, up to 2010, in large and small breast tumour incidence between areas of Denmark which had screening programmes and areas which had not.<sup>1</sup> They conclude that the screening had no effect on large tumour incidence and that there is substantial over-diagnosis. The data presented in the paper, however, indicate the opposite conclusions.

- (1) Table 2 in the paper shows very clearly that in the non-screening areas at ages 50-69, incidence of large tumours increased by 46%, whereas in the screening areas, the incidence of large tumours decreased by 4%. This indicates that the screening prevented large numbers of advanced cancers. The cross-product ratio from Table 2  $((112.2 \times 82.2) / (117.0 \times 120.1))$  gives a reduction in advanced breast cancer associated with screening of 34% (RR=0.66, 95% CI:(0.61-0.71)). Comparisons across age groups are unreliable, since they are necessarily confounded by factors associated with age. For example, changes in neoadjuvant therapeutic practice over time are likely to be age-specific.
- (2) The above also indicates that many of the additional small tumours in the screening areas were not over-diagnosed but were cancers detected at a small size by screening which would otherwise have been diagnosed later as large tumours. Thus the authors' second approach which assumes that the entire excess of small tumours in the screening areas and epochs are over-diagnosed, will greatly overestimate over-diagnosis. Their estimates from the first method, using all cancers, of 9.9-16.4%, will be closer to the truth. Even this will be an overestimate of over-diagnosis, since there will be some screen-detected cancers in the screening areas diagnosed close to 2010 which would have been diagnosed with symptoms after 2010. These are not over-diagnosed but diagnosed early.

Thus the data presented by Jørgensen et al indicate, contrary to their conclusions, that the screening in Denmark has prevented large numbers of advanced breast cancers and has given rise to at worst modest levels of over-diagnosis.

Tony Hsiu-Hsi Chen  
Professor of Epidemiology  
National Taiwan University, Taipei, Taiwan

Stephen W. Duffy  
Professor of Cancer Screening  
Wolfson Institute of Preventive Medicine,  
Barts and The London School of Medicine and Dentistry  
Queen Mary University of London

## References

1. Jørgensen KJ, Gøtzsche PC, Kalager M, Zahl PH. Breast cancer screening in Denmark: a cohort study of tumour size and over-diagnosis. *Ann Intern Med* 2017; 166: doi:10.7326/M16-0270