
Carolyn Nickson, Kate E Mason and Anne M Kavanagh, 30\textsuperscript{th} March 2014

We refer to the letter by Robert Burton, written in response to our recent ecological study which found that screening participation by Australian women aged 70–74 years is associated with a reduced incidence of large (>15mm) cancers and possibly cancers with nodal involvement without a concomitant increase in overall cancer incidence. [1]

Our study examined specific units of analysis (screening participation and cancer incidence by two-year-period and state) to address a research question relevant to the Australian context. The study generated evidence that there is a benefit to extending targeted screening women aged 70–74 years in Australia.

Burton challenges our findings and conclusion by presenting information on: the incidence of breast cancer in the US following the introduction of screening; the mortality benefit of adjuvant therapy according to tumour size and nodal involvement at diagnosis among early-stage cancers; and the prevalence of adjuvant therapy use in Australia. None of this information as presented by Burton invalidates of our findings or conclusion.

US data on the doubling of breast cancer incidence and the 8\% decrease in late stage cancer in the ‘30 years of mammographic screening’ is not relevant. These findings cannot be generalised to our study because, unlike Australia, the US does not have a population-based mammographic screening program. In addition, the US data include all women aged over 40 years, while our study examines women aged 70 to 74 years. As we argue in our paper, as nearly 99\% of BreastScreen participants aged 70–74 have been screened before, we would not expect to observe increased breast cancer incidence with increased screening participation. Our finding is of particular relevance to the Australian screening program, but it cannot be (and was not) generalised to a claim that increased screening of women aged 70–74 years in a different context would not increase population-level incidence.

Burton asserted that we did not provide data to support our statement ‘The known poorer survival for Australian women aged 70–74 years with larger cancers at diagnosis suggests that the effects of screening observed in this study would lead to a reduction in mortality’. Our statement was supported by survival figures according to tumour size for cancers diagnosed in Australia in 1997 [2] (along with the new findings that screening of women aged 70–74 years is associated with a reduction in larger cancers)[1]. More recent Australian statistics for cancers diagnosed in 2006–2010 (well after 1999, the year by which Burton describes adjuvant therapy as optimal) show that survival continues to be associated with both tumour stage and the TNM Classification of Malignant Tumours: for example, the three-year survival for breast cancers diagnosed from 2006-2010 was 100\% for TNM stage 1, 97\% for stage 2, 85\% stage 3 and 42\% stage 4 cancers [3] (and 99\% for localised cancers, 94\% for regional cancers and 64\% for distant cancers [4]). Burton’s claim that the Early Breast Cancer Trialists’ Collaborative Group [5] showed that tumour size (and nodal status) do not influence the impact of adjuvant therapy on mortality from early breast cancer is unsupported given the wide confidence intervals around those results.

Burton argues that ‘Adjuvant tamoxifen can explain the entire observed decline in breast cancer mortality in Australian women aged 70–74 years’, citing his own ecological study which claimed that ‘most, if not all’ of Australia’s mortality reduction can be attributed to adjuvant therapies because the mortality reduction occurred prior to his estimated impact of screening [6]. That study was unconvincing because it relied on too few units of analysis, and used crude statistical methods. This
subjected it to considerable confounding from the many potential determinants of breast cancer mortality with varying exposure levels – and lag times to effect – over the period of interest.

Burton also cited a study showing a high prevalence of adjuvant therapy use in Australia [7], and referenced a website of routinely reported mortality statistics [8], but neither of these support his claim that only tamoxifen has reduced mortality. Like other commentators in this debate [9], we expect that both treatment and screening have contributed to the observed reduction in breast cancer mortality in Australia, and it is difficult to identify their relative contribution. The high prevalence and early adoption of adjuvant therapy in Australia cited by Burton is likely to have led to improved survival. It is also clear from our own rigorous case-control study that Australian screening participants experience an average 52% (95%CI 41% to 62%) reduced risk of dying from breast cancer, in accordance with similar studies from Australia and elsewhere [10].

We agree with Burton that policy changes extending screening to women aged 70-74 years would ideally be informed by the results of a randomised trial. However, RCTs require many years before the results are known, particularly when there is a long lead-time before benefits are seen (as is the case for mammographic screening), and in reality policy development works to much shorter timeframes. Therefore it is important to conduct rigorous observational studies, such as our own, to develop an evidence-base. As stated in our paper, any benefits of screening need to be balanced against potential negative consequences such as overdiagnosis, false positive screening tests and reduced quality of life through earlier cancer diagnosis and treatment.


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