

# Recent results from the two Canadian Breast Screening Trials

*J Med Screen*  
2014, Vol. 21(2) 59–60  
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DOI: 10.1177/0969141314537615  
msc.sagepub.com

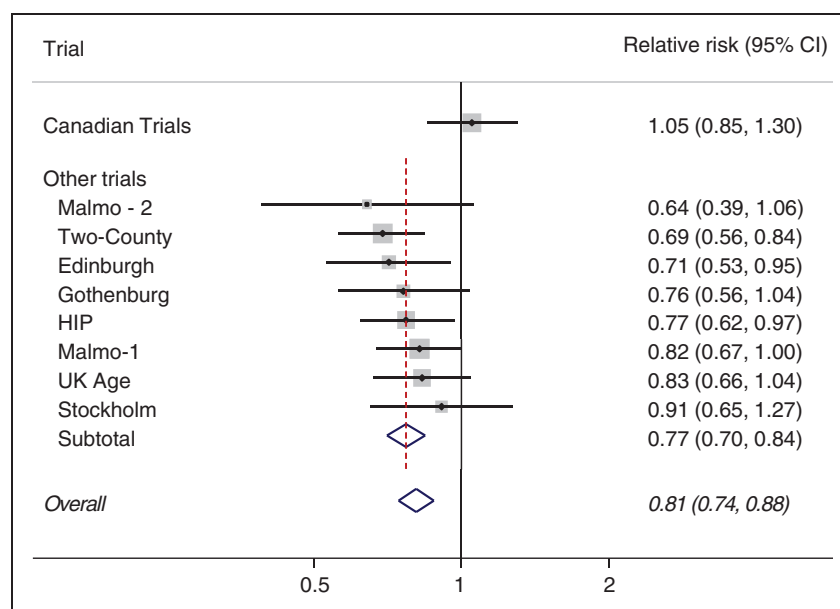


Collectively, the trials of mammographic screening show a substantial and significant reduction in breast cancer mortality among women invited for mammographic screening.<sup>1,2</sup> The two Canadian Trials, NBSS-1 in women aged 40–49 and NBSS-2 in women aged 50–59, are notable exceptions. Neither of these trials showed a significant reduction in breast cancer mortality and a recent update of the two Canadian trials combined shows that this remains the case, with a relative risk of breast cancer death of 1.05 for the mammography compared to the control arm.<sup>3</sup> Figure 1 shows the results of meta-analysis of the most recent published results of the trials,<sup>2,3</sup> including and excluding the Canadian trials. These show a combined 23% breast cancer mortality reduction (RR = 0.77, 95% CI 0.70–0.84) with invitation to screening when the Canadian trials are excluded and a 19% reduction (RR = 0.81, 95% CI 0.74–0.88) when they are included.

Why do the results differ between the two Canadian trials and the other trials? The Canadian trials did not achieve earlier detection in terms of a reduction in incidence of node positive tumours in the mammography arm, a prerequisite for a subsequent reduction in

mortality.<sup>4</sup> However, this in turn begs the question why no such reduction in node positive tumours was achieved? There are several reasons:

1. Firstly, the trials are not of mammography against no screening. Physical examination is a potentially effective method of early diagnosis, and features as part of the control regimen in both Canadian trials. In the 50–59 age group, the offer of annual mammography plus physical examination was compared with annual physical examination; in the 40–49 age group the offer of annual mammography was compared with that of an initial physical examination. In both trials, training in breast self examination was given to the control group. Thus the Canadian trials compare two screening regimens, rather than screening with no screening.
2. Secondly, the technical quality of the mammography in the Canadian trials was poor, as noted by independent reviewers and acknowledged by the trialists themselves.<sup>5,6</sup>
3. The use of randomisation lists in conjunction with initial palpation of all subjects in these volunteer-based trials may have led to non-adherence to the



**Figure 1.** Meta-analyses of the breast screening trials, showing effects of invitation to screening on breast cancer mortality, including and excluding the Canadian trials' results.

randomisation protocol, whereby those with palpable tumours at recruitment had a greater chance of being allocated to mammography.<sup>7</sup> The authors argue that this did not occur,<sup>8</sup> although it is accepted that the lists were changed in the course of the study<sup>9</sup> and there was a significant excess of advanced cancers at recruitment in the mammography arm.<sup>10</sup> Also, as the Canadian trialists themselves note, when prevalence screen tumours are excluded from analysis, a 10% breast cancer mortality reduction in the mammography arm is seen,<sup>3</sup> more consistent with the results of the other trials.

If we give the Canadian trials the benefit of the doubt as regards the randomisation, it still has to be acknowledged that they do not yield a useful estimate of the effect of mammography on breast cancer mortality. They give an estimate of the effect of mammography, probably of poor quality, in addition to that of one or other physical examination regimen. On this basis alone, it is appropriate to estimate the effect of mammographic screening excluding the Canada trials. This would yield a 23% reduction in breast cancer mortality among women offered mammography, or an approximate 35% reduction in mortality in women actually screened.

The editorial accompanying the Canadian trials update calls for yet another review of mammography for policy-makers.<sup>11</sup> This is unnecessary. The Canadian trials have never shown a mortality reduction in their mammography arms and the most recent update does not add to our knowledge on the subject.

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