We are pleased about the general agreement that PBI does not increase breast cancer mortality in comparison with WBI and it is therefore a safe treatment option for suitable patients. PBI with TARGIT-IORT within a risk-adapted approach has the convenience of being completed at the time of lumpectomy, has lower acute and late toxicity[1-3], is preferred by patients[4 5], improves cosmesis and quality of life[6 7], is less expensive[8 9], and reduces environmental and social costs[10]. Common sense would dictate that it should become an accepted treatment option for suitable patients world-wide.

As stated in our paper, we included only *published randomised* trials that compared PBI vs WBI *and* reported 5-year mortality data. Amongst all search results, every trial that fulfilled these criteria was included. The number of deaths and 'proportion of patients with mortality events' were all at a median follow up 5-6 years.

We chose to emphasise the absolute difference (and 95% CI) rather than hazard ratio, as this gives the exact rather than the relative value, and is the most relevant clinical statistic. To put it in perspective, we have also mentioned how the difference is a large proportion of the total mortality: a 25% reduction in mortality with PBI.

With a large number of randomised patients (n=4251), and a low overall mortality (n=207), the observed difference between PBI and WBI was 1.3%, favouring PBI. The p-values tell us that if in reality the difference were zero and PBI and WBI led to identical mortality, then the probability of observing a difference of 1.3% favouring PBI, is p=.05 by the random effects model; the corresponding probability using the fixed effects model is p=.13. Given that both the probabilities are low and taking into consideration that both models found a definite reduction in non-breast-cancer mortality with PBI, but no difference in breast-cancer mortality, it is clear that there is really no meaningful discrepancy between the results of the two models, and both support the conclusions.

Higgins I^2 values for heterogeneity were 15.2%, 6.6% and 9.4% for non-breast-cancer, breast-cancer and total mortality. These low I^2 values demonstrate a low level of variation across the studies due to potential heterogeneity and also counter the final point by showing that the results are not 'largely driven by the TARGIT-A results'.

This meta-analysis confirms that mortality benefit we first reported in the TARGIT-A trial[11] is consistent across other trials of PBI. The correspondents ask why this small difference, detectable in modern trials, was not seen before. As previously suggested[12], in older trials over 50% patients died from breast cancer in the first 5 years[13] and a 1-2% difference wouldn't be detectable until breast-cancer mortality reduced in the later years. On the other hand, in these modern trials, <5% patients die – more than half of these from causes other than breast cancer. So a 1.3% difference is not only statistically detectable, but given the large number of breast cancers being treated, it is clinically important enough for us to consider a change of practice.

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