Author's response to reviews

Title: Comparative benefit from small tumour size and adjuvant chemotherapy: clues for explaining breast cancer mortality decline

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Version: 3
Date: 28 March 2014

Author's response to reviews: see over
Dear Editor-in-Chief,

I am sending the manuscript **Comparative benefit from small tumour size and adjuvant chemotherapy: clues for explaining breast cancer mortality decline** for publication in the *BMC Cancer*.

Breast cancer mortality is slowly and steadily declining in Canada, USA and several countries of Europe. Such reductions have been attributed largely to the prolongation of life among women with the disease. Improvements in early detection and/or improvements of treatments are currently accepted as leading explanations for the mortality reduction.

Analyses of factors responsible for the observed breast cancer survival improvement are difficult to conduct on a population basis because tumour registries often have little information on characteristics of women, their tumour and treatments. Without such information, it is impossible to disentangle the effects of early detection from that of treatments, while simultaneously taking into account secular trends in characteristics of women or their disease. The question has also been addressed by mathematical models for which, however, slight variations in modelling assumptions can result in marked changes in estimated effects, even when common sources of data are adopted.

Although there is a wide amount of debated issues related to screening mammography effectiveness, smaller tumour size at the time of diagnosis was observed in every trial that has been conducted. Furthermore, given that a substantial number of breast cancer patients are given adjuvant treatments, there is a crucial question involving the relative improvements in patient prognosis resulting from the reduction in tumour size and the administration of systemic treatment when jointly accomplished.

In this report, we indirectly approached this question by assessing adjuvant treatment effectiveness according to tumour size at diagnosis in an "experimental" setting i.e. in a randomized clinical trial comparing adjuvant chemotherapy to no post-surgical systemic treatment. Findings reveal that there is a different time-dependent benefit from chemotherapy and from smaller tumour size at diagnosis. The benefit from adjuvant chemotherapy is long-lasting for patients with any tumour size while the early benefit of diagnosing smaller tumours substantially decreases afterwards.

In conclusion, the results of our study, evaluating tumour-size-related prognosis changes in a particular setting, suggest that the effect of tumour size on the mortality reduction may be limited to the early post-surgery time in comparison with the corresponding effect of adjuvant therapies, which seems to play a more prominent and long-lasting role.

Best regards.

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