Screening and Breast Cancer Mortality—Response

Carolyn Nickson¹, Kate E. Mason¹, Dallas R. English², and Anne M. Kavanagh¹

We write in response to the letter from Bell and Burton regarding our article (1).

Bell and Burton question the results of case–control studies because of potential confounding arising from differences in breast cancer risk between women who do and do not participate in mammographic screening. In our study, we included 2 potential confounders—socio-economic status and rurality—which made a negligible difference to our estimates (adjusted OR 0.48, unadjusted OR 0.50). We also conducted “external adjustment” to assess bias due to unobserved confounders (2) for 2 other potential confounders (family history and hormone replacement therapy use), again with negligible change to the results (OR 0.49 and 0.45, respectively). Another potential confounder in Australia is ethnicity: for example, women born in Asia have low breast cancer mortality (3) and women speaking Asian languages at home are less likely to participate in screening (4); however, ignoring this confounder would only bias our OR toward unity.

We have further assessed possible effects of confounding by applying external adjustment for an unobserved, binary confounding variable U. For various combinations of prevalence of U in screened and unscreened women, we estimated the breast cancer mortality OR for U required to adjust the breast cancer mortality OR for screening from 0.48 to 0.80 (Table 1). We found, for example, if the prevalence of U is 20% in screened women and 30% in unscreened women, the OR for U would need to exceed 10, and if the OR for U were 2.0, the prevalence of U in screened versus unscreened women would need to differ greatly (20% vs. 90%).

No modeled scenarios seem plausible because, apart from age and rare high-risk genetic mutations, most risk factors for breast cancer have relative risks less than 3.0 (5), and they are unlikely to also be strong determinants of participation. Mammographic breast density is a strong risk factor (4–6-fold risk; ref. 5), but it is unlikely to confound our results because it is not known by women who attend screening. Therefore, it is implausible that ignoring unobserved confounders will appreciably bias the results toward finding a benefit from screening.

Our study did not evaluate the relative contribution of treatment and screening to mortality declines, nor did it investigate overdiagnosis; we addressed the specific question “Does breast cancer screening, as practiced in a population-based screening program, reduce mortality from breast cancer for women who participate?” As for case–control studies of other countries’ population-based screening programs (1), our study showed that it does. Our findings are robust to adjustment for plausible confounders.

Table 1. OR for breast cancer death in relation to an unobserved, binary confounding variable U required to produce an adjusted OR for breast cancer death in relation to participation in screening of 0.8

<table>
<thead>
<tr>
<th>Prevalence of confounder U in screening participants</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of confounder U in nonparticipants</td>
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<tr>
<td>10%</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.15</td>
<td>0.31</td>
<td>0.41</td>
<td>0.49</td>
<td>0.55</td>
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<tr>
<td>20%</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.01</td>
<td>0.21</td>
<td>0.35</td>
<td>0.45</td>
<td>0.52</td>
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<td>30%</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.01</td>
<td>0.09</td>
<td>0.27</td>
<td>0.39</td>
<td>0.47</td>
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<td>40%</td>
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<td>&lt;0.01</td>
<td>0.17</td>
<td>0.32</td>
<td>0.42</td>
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<td>50%</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.03</td>
<td>0.23</td>
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<td>60%</td>
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<td>70%</td>
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<td>80%</td>
<td>&lt;0.01</td>
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Authors' Affiliations: Centres for Women’s Health, Gender and Society and ME gia Epidemiology, Melbourne School of Population Health, The University of Melbourne, Melbourne, Victoria, Australia

Corresponding Author: Carolyn Nickson, Centre for Women’s Health, Gender and Society, Melbourne School of Population Health, University of Melbourne, VIC 3010, Australia; Phone: 61-3-8344-0785; Fax: 61-3-9347-9824; E-mail: cnickson@unimelb.edu.au

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References

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