Author's response to reviews

Title: Clinical management of women with metastatic breast cancer: a descriptive study according to age group.

Authors:

Klaartje Manders (klaartje.manders@tiscali.nl)
Lonneke V van de Poll-Franse (l.vd.poll@ikz.nl)
Geert-Jan Creemers (mdogcs@cze.nl)
Gerard Vreugdenhil (g.vreugdenhil@mmc.nl)
Maurice JC Van der sangen (maurice.vd.sangen@catharina-ziekenhuis.nl)
Grard AP Nieuwenhuijzen (grard.nieuwenhuijzen@cze.nl)
Rudi MH Roumen (r.roumen@mmc.nl)
Adri C Voogd (adri.voogd@epid.unimaas.nl)

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Author's response to reviews: see over
Maastricht, June 30, 2006

Re: manuscript MS 1766346313846398, third revision

Dear Editor,

We are grateful to the referee, Dr Pandey, and your statistical advisor, Dr Villanueva, for their comments on our revised manuscript. Our response to them and the corresponding changes in our manuscript have been added to this letter. In addition, the text has been copyedited by a native English speaker and a statement has been added about ethical approval. Ethical approval was not considered necessary for our study because it was based on a review of medical charts only and did not include any additional testing of patients.

We look forward to receiving your final decision regarding our manuscript.

Yours faithfully,

Adri C. Voogd, assistant professor of clinical epidemiology

Address for correspondence:
A.C. Voogd, PhD
Department of Epidemiology
Maastricht University
P.O. Box 616, 6200 MD Maastricht
THE NETHERLANDS
telephone: -31.43.388 2387; fax:-31.43.2884128;
e-mail: adri.voogd@epid.unimaas.nl
Minor essential revisions:

1. “However, more research is needed …”. This statement in the conclusion should also be added to the conclusions of the abstract.

Reply:
We have followed the advice of the referee and have added this statement to the conclusions of the abstract as well.

2. Table showing proportion of patients receiving radiotherapy, chemotherapy and hormone therapy, according to age and co-morbidity should be added or provided as additional file.

Reply:
We strongly prefer to adhere to our point of view that a straightforward presentation of the information on co-morbidity in Table 1 is a sufficiently adequate illustration of the potential confounding effect of this factor. Numbers become too small to make a further subdivision within each age group according to co-morbidity and treatment, as is illustrated by the Table on the last page of this letter. Although a quick view might lead to the conclusion that age is a more important factor than co-morbidity regarding the decision for radiotherapy, chemotherapy and hormonal treatment, statistical testing becomes a tricky business because of the limited power of the tests. Therefore we do not support the view of Dr Pandey that including this Table to the paper or providing it as an additional file contributes to a better understanding of the results of our study.

3. As no information is available on hormone receptors all discussions on Table 3 b are redundant. The fact of absence of information in this respect should be mentioned in results page 8.
Reply:
We agree with Dr Pandey that the lack of information on hormone receptor status is limiting the reconstruction of the decision-making process on the use of endocrine treatment and this limitation has been mentioned in the revised manuscript, as was suggested by Dr Pandey. However, despite this limitation, the Table still contains valuable information, such as the lack of an association between age and the use of endocrine treatment and the number of courses inducing any tumor response. We therefore prefer to keep table 3b in.

4. To my knowledge Fishers exact test ….

Reply:
We would like to refer to the comments of Dr Villanueva, the statistical advisor, who considers the statistical procedures and the reporting of the results appropriate.

Reply to the comments of Dr Villanueva:

Minor essential revisions:

1. The authors should specify the level of significance used.

Reply:
The significance level was set at 0.05 for all analyses. We have added this information to the statistical analysis section on page 6.

2+3. The authors should recognize that the small sample size and number of inferences drawn from the data raise the strong likelihood of the multiple comparisons problem…However, the authors will do well to acknowledge this in the Discussion section as a limitation of the study. In addition, the authors should soften their language when speaking of “significant” differences among groups. It is usual to discuss the methodologic shortcomings of the study in the Discussion section. The authors will need to do this. In addition the issue of multiple comparisons the authors may discuss ascertainment bias, the relationship of their study population to the total population, etc.

Reply:
We have followed the advice of Dr Villanueva by adding the following paragraph to our revised manuscript:
“Our study has several limitations. First, when considering the results it should be realized that the number of patients was small and that the large number of tests for possible associations carries the added risk that apparently significant differences will occur by chance alone. Second, our study is based on patients treated in two non-
academic, teaching hospitals and it is not sure that comparable results would have been obtained for patients treated in an academic centers or in smaller non-teaching hospitals.” In addition, the use of the word “significant(ly)” has been reduced to an absolute minimum (4 times in the whole manuscript).

4. It is unnecessary to specify the statistical test used to arrive at the p-value in tables.

Reply:
We have deleted the statistical test used from the tables in our revised manuscript.
Table. Proportion of patients receiving radiotherapy, chemotherapy or hormonal treatment, according to age group and co-morbidity.

<table>
<thead>
<tr>
<th></th>
<th>Radiotherapy</th>
<th>Chemotherapy</th>
<th>Hormonal therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20-49</td>
<td>50-69</td>
<td>70+</td>
</tr>
<tr>
<td>CVD</td>
<td>100% (1/1)</td>
<td>74% (17/23)</td>
<td>50% (6/12)</td>
</tr>
<tr>
<td>Lung Disease</td>
<td>100% (5/5)</td>
<td>63% (5/8)</td>
<td>60% (3/5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>-</td>
<td>80% (4/5)</td>
<td>43% (3/7)</td>
</tr>
<tr>
<td>No comorbidity</td>
<td>72% (18/25)</td>
<td>68% (19/28)</td>
<td>0% (0/4)</td>
</tr>
</tbody>
</table>