Author's response to reviews

Title: From the set-up of a screening program of breast cancer patients to the identification of the first BRCA mutation in the DR Congo

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Author's response to reviews: see over
Dear Mrs Aguirre

We refer to your e-mail of June 16, 2014.

As requested, please find hereafter our point-by-point response to the additional concerns of referee 1, Dr M Mena.

We wish you good receipt of our cover letter and revised manuscript (with changes/responses to the reviewer highlighted and additional language editing in red) and look forward hearing from you.

Yours sincerely

Prof C Van Ongeval

Enclosure: Responses to comments of referee 1

PS We would like to draw your attention to the fact that Dr Mena refers, again, to figure 5 as the figure entitled “Distribution of breast cancer for the different age categories”, but in fact this is, in our text, figure legends and figure files figure 4.
Responses to the concerns of referee 1 (reviewer: Marisa Mena)

Thank you again for reading and improving the manuscript! Whilst implementing the previous comments in the paper, unfortunately new mistakes have been made; we apologize for the extra work this has caused.

Abstract

- In the methods section all the activities undertaken should be described, including the clinical breast examinations, the referrals and diagnosis of encountered lesions and BRCA testing, at least in a general way.

Response

In response to your comment, we have adapted the text as follows:

“... clinical, technical and social aspects of breast cancer. Different channels were used to inform women about the campaign and clinical data (on medical and family history) were collected. The participating women were investigated with clinical breast examination by the awareness group. Women in whom a palpable mass was detected were referred to the hospital: they received a mammography and ultrasound and – in case of suspicious findings – additionally a core needle biopsy. In case of a positive family history, a blood sample was taken for genetic investigation.”

Because of this additional text the maximum of 350 words (allowed for an abstract) was however exceeded; therefore we had to delete a few words/sentences in the rest of the text of the abstract.

Introduction

- Globocan 2012 are estimations, this is important to be specified.
- In the last sentence of the first paragraph, where this increase (from 19 to 25.5) has been observed must be indicated
- In the first paragraph the sentences indicating the Age Standardised Rates are not well described, please check (i.e. ASR should not appear after the numbers)

Response

As all these observations are correct, we have changed the text as follows:

“An estimated total of 1,676,633 females were diagnosed with breast cancer globally in 2012 corresponding to an age standardized breast cancer incidence rate worldwide of 43.3 cases per 100,000 women and a mortality rate of 12.9 per 100,000, while in Europe the incidence rate of breast cancer is 94.2 per 100,000 and the mortality rate 22.4 per 100,000. [1] In contrast with Europe the incidence rate in Sub-Saharan Africa is 25.5 per 100,000 and
the mortality rate 19.3 per 100,000; for the Democratic Republic of Congo (DRC) the incidence rate is 23.5 per 100,000 and the mortality rate 14.2 per 100,000, showing a 4 times lower incidence but slightly lower mortality rate. In 2012 occurrence of breast cancer increased from 19 to 25.5 per 100,000.
Considering population growth and aging, the incidence in breast cancer rates is rapidly increasing in Africa. In Uganda, for example, breast cancer incidence rate has ..."
• RDC must be spelled the first time that it appears in the text, like in the abstract.

Response
Has been corrected.

• Some sentences are redundant and sometimes inconsistent between them, for instance in the fourth paragraph the authors mention that “the recording of the occurrence of breast cancer is important to obtain a correct view on the prevalence of these cancers” and later “in the absence of cancer registration, the incidence of cancer is not known”, please check

Response
In response to your comment, we have removed the sentence “in the absence of cancer registration, the incidence of cancer is not known”.

• Also the two last paragraphs of the introduction contain some redundancies and should be merged in one and presented as the aim of the study. In the resulting paragraph is important to mention the country, DRC. Further details must be provided in the methods sections and not here.

Response
We agree with your comment; as a matter of fact the method elements do not need to be described in the introduction section.
Therefore we have removed “We used this information to build set up the awareness program. The program was started in Kinshasa as this was the only place where mammographic equipment and radiological expertise was available at the department of medical imaging of the GHK. Since no financial support was available, it was decided to use BSE and CBE as screening tools while biopsies were only performed in the case of suspicious lesions.”

As suggested, we have also added the country, DRC, to the aim paragraph: “The aim was to design a breast cancer awareness campaign in the DRC, based on information (on early signs of breast cancer), education (on BSE and CBE) and diagnosis. The program was initiated by an interdisciplinary working group including oncologic surgeons, radiologists and nurses.”

• There are several structural mistakes, for instance references should be properly indicated with a number (Vancouver style) which refers the reader to the reference section and not displayed in the text (e.g. (http://www.who.int/cancer/nccp/en/), http://portal.bhgi.org/pages/default)

Response
We have made the necessary changes.

Methods

• In the methods section the expert group is described as having 3 persons but in the flow diagram there are four.

Response

This does not correspond indeed. As the supervising technician was part of the expert group we have changed the sentence in the text as follows: “The expert group consisted of a radiologist, a surgeon/oncologist, a gynecologist and a technician.”

• The sentence “The BHGI and the WHO both described the need for the study of local cancer population, described by Bridges et al as “developing evidence. [15]” does not belong to the methods section and it should be omitted.

Response

As requested, this sentence has been omitted.

Results

• The flow diagram has consistently improved, but still needs to be reviewed: The boxes corresponding to the different channels to present the campaign (TV, radio, women organizations, churches and attendees inform neighbors, family members) should be all placed at the sides of the narrow going from the box of the awareness group to the number of women reached, in order to differentiate them from the boxes corresponding to the participants of the studies, and in a way showing that they are at the same level. From the box “Total women reached” (n=4315) should arise another box “Total women examined” and then the sum of the number of palpable lesions + no palpable lesions should correspond to them. The box corresponding to “mammograms in the hospital” since is a activity in parallel should not come from the box of the 4315 women reached.

Response

As requested, we have made the necessary changes.

• The authors indicate that one out of 100 malignant lesions was excluded but just after they state that 87 were invasive and 13 in situ, which sums 100. Please correct.

Response


This is indeed an appropriate remark; therefore this number has been corrected in the text:

1. In the results section: “One malignant lesion was excluded from the whole study as only cytology was performed to diagnose the lesion. Of the 167 lesions which were correctly biopsied, 100 were found to be malignant, 66 were benign lesions, 1 was normal.”

2. In the discussion section: “More than one thousand (1,113) radiological breast examinations were performed: 167 were concluded as BIRADS 3, 4, 5 and 100 cancers were detected (59% true positives).”

Discussion

- I am not sure that the difference between the detection rates of breast cancer in Sudan and RDC can be only attributed to better training in RDC, the sentence should be reformulated as not as clear, other reasons are possible and must be listed.

Response

Thank you for drawing our attention to this. We have changed the text as follows:

“This difference can be attributed to the training of the health care workers in the awareness group of Kinshasa (better trained), the educational status of the women (rural versus non-rural situation) and to more practical issues (accessibility to the hospital).”

- The purpose of Mena’s paper is not indicated thus the paragraph comparing the results with it is confusing

Response

We have corrected this as follows:

“... awareness campaign. This is in accordance with the findings of Mena et al. on the assessment of the impact of the Ghanaian non-governmental Breast Care International program on knowledge, attitudes and practices toward breast cancer in rural Ghana. In this paper the investigator concluded that the knowledge of the referent group on breast cancer appearing as a painless lump was only 53.3%, compared to the 82.3% of the.......”

- The comparison highlighted in yellow is not clear and should be reformulated.

Response

We agree with your comment. On second thoughts, we have decided to omit this sentence as it adds nothing to the discussion. We hope you agree.

Figures
The y axis of figure 5 is misleading, are the bars numbers or percentages? Please clarify it by adding a proper label and the number and/or the percentages over the bars.

Response

As requested we have added a proper label (numbers instead of percentages) and numbers over the bars. We have also added these figures in the results section.

Figure 4 - Distribution of breast cancer for the different age categories

References

• Globocan 2012 is not properly referenced, please check.
• Some references contain mistakes, please check.

Response

References have been checked, as requested.

General

• English and general editing is highly required.

Response

We have made several additional corrections.