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

Authors:

Gertrude Luyeye Mvila (gluyeye@yahoo.fr)
Sandra Postema (sandra.postema@uzleuven.be)
Guy Marchal (guy.marchal@uzleuven.be)
Erik Van Limbergen (erik.vanlimbergen@uzleuven.be)
Fons Verdonck (fons.verdonck@med.kuleuven.be)
Gert Matthijs (gert.matthijs@uzleuven.be)
Koen Devriendt (koen.devriendt@med.kuleuven.be)
Genevieve Michils (genevieve.michils@uzleuven.be)
Chantal Van Ongeval (chantal.vanongeval@uzleuven.be)

Version: 5
Date: 15 May 2014

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

We refer to your e-mail of April 21, 2014.

As requested, please find hereafter our point-by-point response to the concerns of both reviewers.

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

Sincerely yours

Prof C Van Ongeval

Enclosure: Responses to comments of first and second reviewer
Response to comments of the first reviewer

Thank you again for the excellent and legitimate comments; we have adjusted the manuscript as suggested.

Introduction

• Globocan 2012 presents indeed specific information on breast cancer in RDC. Look at country fact sheets by population

We have found indeed results on incidence and mortality of the population of RDC. This information has been included as follows:

In contrast with Europe the incidence in Sub-Saharan Africa is 25.5 ASR per 100,000 and the mortality 19.3 ASR per 100,000; for the RDC the incidence is 23.5 per 100,000 and the mortality 14.2 ASR 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.

• The last sentence of the introduction section (the one referring to the BRCA mutation) is already a result, therefore should be better placed in the results section

This observation is correct and, as suggested, the sentence has been moved from the introduction to the results section: i.e.

“Genetic analysis
One family with breast cancer at young ages was identified. Genetic analysis revealed the presence, in the heterozygous …”

Methods

• The new first paragraph of the methods section (just before the ethics one) belongs to the introduction since is background and should be better placed there

This is indeed correct. We have therefore removed this paragraph from the methods section and (as it summarizes the strategy) modified the introduction section as follows:

“… staffing of advocacy groups.
Based on the information from the WHO, the BHGI and the paper of Bridges et al. it was concluded that health education messages must include the idea that breast cancer is curable in the majority of women provided that it is detected early, diagnosed accurately, and treated appropriately. To optimize successful outcome, communication methods need to be adapted to the cultural boundaries and taboos that invariably surround breast cancer, keeping in mind that those may differ among and within countries, depending on the social context and common healthcare systems.
We used this comprehensive strategy information to build …”

• The flow diagram is a good idea to illustrate the strategy process, but then it should be exhaustive and all the numbers must be fulfilled in each box (e.g. how many people and their profession in the expert group, in the awareness group, how many palpable masses, how many no palpable lesions, how many women without any sign, how many without no info on follow-up) notably from the 4315 women reached to the 167 women referred to the hospital

Of the 4,315 women who participated in the campaign, 497 were found with a palpable mass by the nurses of the awareness group. Meanwhile the number of radiological breast examinations in the hospital increased due to the information about an ongoing campaign on breast cancer which had
an effect on the presence of women in the radiology department (for an additional breast exam) but also on the physicists who were referring women much more easier to the radiology department when a problem of the breast was reported.

From the group with a palpable lesion (n=497) 133 finally came to the hospital where they were all diagnosed with BIRADS 3, 4 and 5 lesions.

From the 1,113 women examined with mammography and ultrasound, in addition to the 133 lesions, another 34 received a diagnosis of BIRADS 3, 4 and 5, which gives a total of 167 lesions with BIRADS 3, 4 and 5 diagnosis.

A lot of effort was made to collect data on the non-presenting women but, due to financial and practical issues, these data were incomplete and therefore not included. The number in the box initially entitled “Referral to the hospital” was the number of women with suspicious lesions; the title and the number were not correct and have therefore been adjusted.

The content has been adjusted as follows:

“The total number of women reached to date amounts to 4,315 and in 497 of these 4,315 women a palpable mass was found by the awareness group (CBE). Of these 497 women 133 consulted the radiology department of the GHK and were all diagnosed with BIRADS 3, 4, 5 lesions. Information on the 364 women with a palpable mass who did not present at the hospital was lost during follow up. Meanwhile, the breast examinations in the GHK increased from 312 in 2010 to 416 at the end of 2012, with a total of 1,113 mammography examinations in the studied period. (Figure 3). Additionally, 34 lesions were diagnosed with BIRADS 3, 4, 5 in patients who were informed about this breast cancer awareness campaign by women out of the awareness group: a total of 167 lesions were biopsied.”

- The sentence “Participants belonged to a wide range of ages” could be better formulated as the range of ages which were included in the study

Thank you for the remark; we adjusted the text as follows:

The range of ages included in the study was from 18 years upwards.

- Still some sentences are already part of the results section and should be rather placed there, such as “one family with breast cancer at young ages was identified” (1) and “Because this is the first attempt to organize a cancer registry, no decisive conclusion on the incidence of breast cancer could be drawn in this study” (2). For the latest, if the authors want to keep it in the methods section the sentence should be reformulated

(1) This sentence has been removed from this section and placed in the results section.

(2) As we prefer to keep this sentence in the methods section, we have reformulated it as follows:

“The collected data were analyzed in order to identify the variations in the etiology of the disease, but because of the study design, no further conclusion on the incidence is made in this study.”

Results

- Table 2 is very important new item to present the results. However, it should be specified in the title that it refers only to the women referred to the hospital (n=167) otherwise is confusing.

We agree with your comment and have changed the title:

“Table 2 - Socio-demographic characteristics of women diagnosed with BIRADS 3, 4, 5 (mammography, ultrasound) in the GHK in Kinshasa and Bas-Congo (DRC)”
**Figures’ legend**

- The figure’s legend is incorrect (e.g. figure 4 is mammograms per year and not figure 3 as it is indicated in the figure’s legend list)

*Has been checked.*

**References**

- Since GLOBOCAN 2012 is reference 1 there is no need to use GLOBOCAN 2008 as reference 2 since the last is outdated

*Thank you, we have removed the reference of Globocan 2008.*

- Since the usefulness of BSE in reducing breast cancer mortality is controversial topic maybe some reference on the pertinence of using BSE in LMIC could be added

As a matter of fact the use of BSE in the European population is not recommended (Thornton H, Pillarisetti RR: ‘Breast awareness’ and ‘breast self-examination’ are not the same. What do these terms mean? Why are they confused? What can we do? European Journal of Cancer 2008, 44(15):2118-2121) but in a letter by Panieri et al (Breast-cancer awareness in low-income countries. The Lancet Oncology 2013, 14(4):274-275), he concluded that “much more need to be done than just willing volunteers and educational campaigns, but to attempt tackle the problem without these interventions (BSE and CBE) would be to omit a cheap, logical and effective first step”. The same conclusion is made by El Saghir et al in El Saghir NS, Anderson BO: Breast cancer early detection and resources: where in the world do we start? The Breast 2012, 21:423-425.

Therefore we have added 3 references in the text:


“The latter group included nurses and technicians who underwent a specific training in clinical examination of the breast, in auto-palpation and provided information and education during the campaign (Toner LCM and Jodrell N: Screening and breast cancer: the role of breast awareness. Journal of Cancer Nursing 1997, 1(2):76-80).”
Response to comments of the second reviewer

Thank you again for the excellent comments; we have adjusted the paper as suggested.

• This is an interesting story but I am unsure exactly what transpired.

The basic concept to start the breast-cancer-awareness program is best described by El Saghir NS (The Breast 2012; 21:423-425) as “Improvement of mortality and reduction of morbidity from breast cancer in LMCs must be achieved by down-staging breast cancer at diagnosis. Discovering breast cancer at earlier stages is achievable by raising awareness, teaching BSE, promoting CBE, and screening mammography when they become able to afford it and have the infrastructure to do it. Current awareness campaigns will pave the way for it.”

Our first goal was to inform women of Kinshasa on breast cancer because, due to financial and psychological issues (fear of mastectomy), a lot of women were and are still seeking help with witchcraft. The work of the expert group and the awareness group resulted in an increase of women consulting the hospital for additional care; most of the women who reported a palpable mass were diagnosed with malignant disease at stage III. The second goal of the campaign was to inspire officials and local authorities to put breast cancer care on the agenda of women’s health.

• In particular the authors describe 100 breast cancers discovered among 4315 women. This is a very high prevalence indeed (1). who are these women. how where they selected (2). what exactly is the protocol (3). The paper is best described as a non-randomised trial of clinical breast examination and should be presented as such (4)

Thank you for this important remark.

(1) ‘This is a very high prevalence indeed’
We cannot conclude anything on the real prevalence. The high number is probably related to the extra motivation of women, who already knew they had a breast lump, to participate in an awareness campaign. It can be compared to the higher prevalence of breast cancer described in the first screening round of a mammography screening programme.

We have added this in the paper as follows:
Information on cancer and BSE together with BCE resulted in a better recognition of the early signs of breast cancer. The high amount of positive examinations can be compared to the high incidence of breast cancer in a first screening round in a population-based mammography screening program or/and is a result of women who already felt a lump but for whom the given information was the extra motivation to participate in an awareness campaign. This is in accordance with …

(2) ‘Who are these women? How were they selected?’
The women were not selected, they were only invited to come to churches or women organizations where the awareness group was presenting the information on breast cancer.

(3) ‘What exactly is the protocol?’
In the Methods’ section the strategy of the campaign is described in a flow diagram explaining the practical organization (Figure 1).

(4) ‘The paper is best described as a non-randomised trial of clinical breast examination and should be presented as such’
In response to your suggestion to describe this paper as a non-randomised trial: we consider this campaign rather as a retrospective, descriptive analysis of a standard-of-care project (i.e.
because, first of all, the focus of the campaign was to provide information to women who would normally turn to witchcraft and, secondly, because of the way the program was organised.