Author's response to reviews

Title: Incidence of cancer among residents of high temperature geothermal areas in Iceland: A census based study 1981 to 2010

Authors:

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Version: 2 Date: 24 August 2012

Author's response to reviews:

Dear Editor,

We are thankful for the comment from the reviewers and hope we have been able to take into account the views of the reviewers. Our responses are highlighted with bold font (our page numbers in the letter refer to the marked copy of the text):

Reviewer's report

Title: Incidence of cancer among residents of high temperature geothermal areas in Iceland: A census based study 1981 to 2010

Version: 1 Date: 31 July 2012

Reviewer: Peter Baxter

Reviewer's report:

My comments are focused on the geothermal aspects of the paper as I'm not sufficiently well versed on epidemiological research into cancer aetiology in Iceland to know if this paper represents a significant advance in the use of cancer registry data in that country. It is well written and presented and although I'm not a statistician the approach to the analysis and the role of potential confounders seems thorough. It is an interesting question whether living in volcanic areas presents any special health risk or advantage and the literature is sparse on this matter. This paper is therefore welcome. However, the weaknesses lie in the absence of exposure data and in the extent of moving residence during the follow up period, the latter being mentioned in the text. Indoor air radon is the main issue in drawing any conclusions on a link between this gas and cancer incidence, as has been indicated in the abstract conclusion (which for clarity should be slightly reworded and softened), yet this is not mentioned except for a passing reference to the low
radon levels found in geothermal water in Iceland on page 3. Hot water with these low levels is used in homes for bathing, showers, etc, but not for drinking, and presumably no surveys on indoor radon have been undertaken in Iceland (which is surprising) or they should be referenced here. It would be important to have this clarified and why, if the concentrations of radon are likely to be so low, the authors attribute so much weight to it being a causal factor in explaining the variation in cancer incidence they have found.

We have now reworded the conclusion in the Abstract, page 2, by adding comment on the lack of radon measurements and mentioned the possibility of unknown confounding factors to our findings. Consequently we have made the same changes in the main text in Discussion, page 18.

At present the evidence for such a hypothesis looks very weak, especially as they say there is no increase in lung cancer given the known interaction between radon exposure and tobacco smoking.

We agree with the reviewer, however would like to point out that we have now added more precise information on the smoking habits of the studied populations, which show that the proportion of never smokers is highest in the high-temperature geothermal areas. Nevertheless there is a non-statistical significant increase risk for lung cancer in the high-temperature geothermal areas. The new information on smoking habits is supplemented in a new section in Discussion, page 14.

The authors do not mention the role of chance when making multiple comparisons with a long list of causes of death and finding statistical significance. The increases in cancer incidence by cause are non-specific and modest.

To meet this point we have added a sentence and a reference in Discussion, page 16.

The titles of the three tables do not explain that Table 2 is all deaths combined, table 3 is men only and Table 4 is women only. I have two slightly different forms of Fig. 2 which is a mistake, presumably.

We have now added clarification to the heads of Tables 2 to 4. Our mistake in the different forms of Figure 2, has been corrected.

I’m in favour of publishing this paper if the above comments can be adequately dealt with as it would contribute to answering a question which is frequently asked in volcanic areas yet few studies have been previously undertaken. Radon may a red herring and other exposures related to geochemical, dietary and even
occupational factors in these rural (farming) communities so far unknown may be specific to certain volcanic areas and worthy of future hypothesis generation.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
No competing interests to declare

Reviewer's report

Title: Incidence of cancer among residents of high temperature geothermal areas in Iceland: A census based study 1981 to 2010

Version: 1 Date: 20 July 2012

Reviewer: Suminori Akiba

Reviewer's report:

Authors observed an increased cancer incidence among residents in the high temperature geothermal areas. An increased cancer incidence was observed for cancers of the pancreas, breast, lymphoid and hematopoietic system. Hodgkin lymphomas and basal cell carcinoma were also increased. Since the increase was observed even when they used the warm reference area for comparison, it is not due to the difference of temperature in the exposed and control areas. The observed increase cannot be explained by smoking, either, since the lung cancer risk was not much increased among residents in the geothermal areas. Smoking cannot explain the excess cancer of breast cancer, which is known to be only weakly related to active smoking, if at all. The absence of lung cancer risk among men also makes it unlikely that radon gas exposure caused observed increase of cancers.

Authors suspects that pancreas cancer is increased by radon gas exposure. However, as already pointed out, the fact that lung cancer risk did not increase indicates a lack of significant exposure to radon gas and it decay products. It is also of note that a pooled analysis of 10 studies of underground miners exposed to radon showed an O/E of 1.05 for pancreatic cancer (IARC monograph 78).

In the study we refer to the IARC monograph 78 (our ref. number 14). The O/E ratio 1.05 for pancreas mortality in the monograph is obtained from the study of Darby et al 1995 (our ref. number 20), that study we refer to in the section
discussing the pancreas cancer incidence. To meet this point of the reviewer we
have added this O/E ratio in Discussion, page 12.

Authors may suspect that the observed increase of pancreatic cancer was
caused by exposure to water radon. However, as pointed out by Kedall and
Smith (J Radiol Prot 2002;22:389–406.), the highest organ dose from ingested
radon is to the stomach, which receives 90% of the total effective dose. The
absence of an excess stomach cancer risk in the present study does not support
the involvement of radon in water.

The geothermal water was not used as drinking water (containing small amount
of radon), which we stated in Methods, page 5, and we agree with Peter Baxter
that if radon plays a role in the exposure that is presumable through indoor air
radon not from ingested radon.

Authors may suspect a radon exposure to the skin and the breast from radon
daughters attached to the body surface when taking bath. In the case of the
breast, however, it is unlikely that radon on the body surface give a significant
dose to breast cancer stem cells since alpha particles are stopped by the skin
(since it has a low permeability).

We agree with the reviewer that it is unlikely that radon on the surface of the
body would contribute to radiation dose to the breast tissue and we do not
suggest that exposure mechanism in Methods or Discussion. This comment is
related to previous comment of the reviewer.

Anyway, if authors suspect the involvement of radon exposure, they should
present estimated radiation doses from such an exposure and discuss whether
that dose is large enough to explain a 59% increase of breast cancer risk.

In this point the reviewer highlights the lack of exposure surveys on indoor radon
in the study like Peter Baxter in his first comment. We have because of these
comments reworded and softened the conclusions in Abstract, page 2, and
Discussion, page 18.

Authors should pay more careful attention to factors other than radiation. Is there
any possibility that women in the geothermal areas tend to stay indoors and
therefore they are more likely to be exposed to passive smoking, which is
strongly suspected to increase a breast cancer risk? The increase of lung cancer
risk by 24% (when compared to warm reference area) among women is
compatible with that idea. – Note that I have no intention to argue that the
observed increase is due to passive smoking. I am trying to indicate that authors
should make discussions regarding such possibilities. It cannot be denied that
each cancer is caused by different factors, rather than radiation.

We have now added more and detailed information on smoking habits according to the different population in the study in Discussion, page 14. Further more we have mentioned the possibility of unknown confounding of the results in Abstract, page 2, and Discussion, page 18.

Authors wrote that the best known etiological factors for bone cancer are ionizing radiation, radionuclides and x-ray therapy. However, I do not think that bone cancer is strongly related to external exposure to ionizing radiation, including x-ray.

We have now added reference concerning the etiological factors for bone cancer.

Level of interest: An article of limited interest
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare that I have no competing interest

Reviewer's report
Title: Incidence of cancer among residents of high temperature geothermal areas in Iceland: A census based study 1981 to 2010
Version: 1 Date: 24 July 2012
Reviewer: Fabrizio Bianchi
Reviewer's report:
The paper is very well done, well designed the investigation, reachly described and clearly reported pros and limitations.
I have only to suggest to improve the discussion about breast cancer results adding the issue of the screening policies, just to ensure the readers that there are no differences in the three different compared areas.

In Iceland screening with mammography have been offered to all women 40 to 69 years of age since 1987, and there are no indications of differences in participation in the screening program according to residency, outside the capital area. This section has been added in Discussion, page 13.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare that I have no competing
We hope we have now responded to all the comments of the reviewers.

Yours sincerely, Vilhjalmur Rafnsson