Authors’ Response to: Skin cancer as a marker of sun exposure—a case of serious immortality bias

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We thank Theis Lange and Niels Keiding for their interest in our report on the risk of skin cancer as a marker of sun exposure and risk of myocardial infarction, hip fracture and death from any cause.1

Most studies are susceptible to certain biases, and inappropriate accounting of person-time in the design and analysis may in cohort studies introduce immortality bias. To address this and other potential biases, the data in our study were analysed both in a cohort design (prone to immortality bias) and in a case-control design, where each case was matched with five general population controls on the basis of age, birth year and gender (Tables 2 and 3 in the paper, respectively), and furthermore using both designs in age-strata of 10 years (Figures 2 and 3 in the paper, respectively).1 In the matched case-control design, immortality bias is unlikely to be present, simply because both cases and controls had to be alive to the same age to be included for further follow-up. The directions of the risk estimates from the two different designs were similar, but effect sizes were attenuated in the matched case-control vs the cohort design, which is why we only concluded on the direction of risk estimates.

In Figure 1 below, we have now performed additional analyses in an attempt to exclude immortality bias using a modified approach. Within 10-year, 5-year and 2-year age-strata, we compared individuals diagnosed with non-melanoma skin cancer within a given age-stratum with those alive and without non-melanoma skin cancer in the same age-stratum. Importantly, those who develop non-melanoma skin cancer beyond the age-stratum enter into the analysis as not having non-melanoma skin cancer. We then followed these two groups for all-cause mortality within each of the age-strata shown in the figure. The results of the analyses are similar to those reported in the paper, to us suggesting that non-melanoma skin cancer is associated with reduced death from any cause.

Interestingly, our results are in line with previous studies on non-melanoma skin cancer and all-cause mortality.
in the Danish general population using similar databases: Jensen et al. have in two studies shown that individuals with basal cell carcinoma have reduced all-cause mortality.\textsuperscript{2,3}

We also thank Theis Lange for his contribution to the discussion of the interpretation of our results in the national Danish media. The national Danish newspaper \textit{Politiken} reported our findings as the main front page story on 16 October 16 2013 under the headline ‘Sunbathers live much longer’. The headline was decided exclusively by the newspaper, and we accepted the main text which in a simplified manner reported on our findings and even mentioned that no causal inference from sunbathing and skin cancer to myocardial infarction, hip fracture or death from any cause could be drawn from our study. An accompanying story focused on the Danish Cancer Society’s yearlong advice to avoid being in the sun, due to the risk of skin cancer. A representative from the Society acknowledged that it is well known that those with skin cancer live longer. She also mentioned that the Society attributed longevity among those with skin cancer to more leisure time outdoor physical activity, rather than to positive effects from sunshine per se.

The Danish public, journalists at national TV and radio, and users of the internet etc. enjoyed the story, and soon almost everybody in Denmark knew that ‘the more you are in the sun, the longer you live’, a clear over-interpolation of our data. This is how stories sometimes develop in the media, beyond the scientist’s control. Due to the high northern latitude of Denmark, Danes are deprived of sunshine for most of the year, and have for the past several years been told to stay away from it even when it is finally there. Therefore, many people in Denmark liked to be told that it was okay to be in the sun for a while, that is without the need to feel guilty.

As a consequence of this massive media attention, many prominent scientists in Denmark, including Theis Lange, read our paper and commented on its limitations (flaws, incorrect analyses etc.) in the media. In other words, our paper got a second round of revision after the one initially provided by the \textit{International Journal of Epidemiology}. As science must often improve by peer review, we much appreciated this further review as well as the opportunity now to respond to the letter by Theis Lange and Niels Keiding.

We are very cautious with respect to analyses and interpretation of national register data, and sincerely welcome advice on how to do this better in the future. Analyses will probably never be ‘correct’ and unequivocal. There are many possible pitfalls and potential biases, and careful thinking and many sensitivity analyses are often necessary when dealing with such data, as in present and previous studies.\textsuperscript{4}

Rereading the paper, the results presented there in Table 3 and Figure 2, which are most likely unaffected by immortality bias, should have been presented in the abstract; however, we were restricted by a word count limit. Also, a discussion of immortality bias would have improved the paper and we are therefore happy to have this opportunity to address this. That said, we believe that the totality of data presented support the conclusion of our paper, which is that having a diagnosis of skin cancer is associated with less myocardial infarction, less hip fracture in those below age 90 years and less death from any cause, as the analyses not prone to immortality bias also support these conclusions.

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**References**