Author's response to reviews

Title: Risk factors for nasal malignancies in German men - The South-German Nasal Cancer Study

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Author's response to reviews:

Re: MS: 1315774931721954
Risk factors for nasal malignancies in German men - The South-German Nasal Cancer Study
Dear Mr. de Jesus,

In responding to three reviews of our manuscript I would address the various topics as follows:

A. Reviewer W. Hoffmann

Major compulsory revisions:

1. Prospective case-ascertainment: It is explained in the methods section, why a prospective case ascertainment was impossible.

2. Origin of histo-pathologic findings: it is explained in the methods section that these informations were provided by the cooperating tumour registries and by respective ENT departments.

3. Use of proxy interviews: This problem is explained in a new section on “Analysis of potential biases”. A new table (8) displays comparison of major risk factor distributions in interview in cases vs. interviews in next-of-kin, demonstrating that for all risk factors but exposure to hardwood dust there is no statistically significant difference.

4. Possible bias due to difference in educational attainment in cases vs. controls: This problem, too, is covered in the new section. An additional analysis (s. table 9) demonstrates that for most of the major risk factors, except for the use of insecticed in homes, prevalences are significantly larger in less educated men. It
is also explained that due to individual habits as well as exposure-prone occupations it was to be expected that cases were less well educated than controls.

5. The question if the data base for cases is population-based is answered in the methods section insofar as cooperation of all ENT hospitals, treating nasal malignancies in the Federal State of Baden-Württemberg, was achieved. In Bavaria case-ascertainment was done by those two tumour registries covering the population of Bavaria.

6. Table 1: p-values are added for distribution of cases vs. controls.

7. Table 2: There have been some typing errors which have been corrected. In addition in the section on the impact of quitting smoking there was a major error due to an until now undetected inconsistency of interview data (actual smokers who indicated that they quit some years ago). As the number of actual smokers is the complement of all ex-smokers the inclusion of actual smokers into the logistic regression was an error of judgement. This has been corrected, the respective part of the table has been recalculated. The result that ex-smokers who quit more than 28 years ago had a significantly lower risk than never-smokers is discussed in the discussion part of the manuscript.

8. Two models applied for calculation of risks: Obviously there are two different views among reviewers. Reviewer Hoffmann would like more explanatory analyses for confounders whereas reviewer Wing questions the rationale for two models. We solved this discrepancy in displaying exclusively results for the full model without p-values. This is well in accordance with the majority of publications of case-control studies.

Minor revisions: Were dealt with according to suggestions of the reviewer.

B. Reviewer S. Wing

1. Para 2 and para 3 are corrected according to suggestions of the reviewer.
2. Details of exposure assessment: It is explained in detail how exposures were ascertained in a most differentiated questionnaire.
3. P 7: The reviewer qualifies our use of the term “quantitative exposure” as not to be correct and suggests to describe the assumption of a linear dose-response relationship instead of. We maintain that “quantitative exposure” is an appropriate term. When regarding the results of analysing exposure to organic solvents (table 6) the tertiles of exposure do in no way show a linear dose-response relationship but indicate a bimodal distribution of risk. However, the analysis by tertiles of exposures is still a quantitative one.
4. Justification for displaying two different models of analysis: There is in fact no justification. We dealt with this remark in omitting model 1 as well as p-values.
5. Discussion: This part of the manuscript has been shortened, omitting sections that were not essential to discuss relevant results.

C. Reviewer M. Röösli
1. Effects more pronounced in smokers than in never-smokers: This topic is covered in the discussion.
2. Shortening the discussion section: Has been accomplished.
3. Formulation of conclusions: The wording has been changed following the suggestions of the reviewer.
4. Selection of controls: This is explained in more detail in the methods section, covering all of the remarks of the reviewer.
5. Minor revisions: Are dealt with according to suggestions of the reviewer, where appropriate.

As the reviewers remarked on insufficient usage of English we asked Edanz to edit our manuscript.

We hope that these modifications of our manuscript now justify the publication in BMC Cancer.

Yours sincerely

Eberhard Greiser, MD, PhD