Author's response to reviews

Title: The association of smoking status with healthcare utilisation, productivity loss and resulting costs: results from the population-based KORA F4 study

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Version: 4 Date: 22 April 2013

Author's response to reviews: see over
To the editorial office of
BMC Health Services Research

Dear Editors,

Thank you very much for providing us with the opportunity to revise our manuscript and re-submit.

We are also grateful to the reviewer for their helpful comments. We revised the manuscript to address these comments, and we think that the concerns were addressed satisfactorily. Please find attached point-to-point responses to the comments and the revised manuscript.

We believe that these changes increased the quality of our paper, and we hope that you will consider the article for publication in BMC Health Services Research.

Thanking you and looking forward to hearing from you soon.

With kind regards,

Margarethe Wacker
Author's response to reviews

Reviewer's report 1

| Title: The effect of smoking status on healthcare utilisation and costs: results from the population-based KORA F4 study |
| Version: 2 Date: 13 December 2012 |
| Reviewer: Marta Trapero-Bertran |

Reviewer's report:

Dear authors,

The question posed is important, well defined and original in your context. The data sounds well controlled, though not much details have been given in your paper about how you have dealt with non-responses (blank responses). The interpretation for the bottom up approach is well balanced with the data, though in terms of comparing your results with other published papers using the top-down approach, I think you should have look and discuss these extensively in the discussion section. Specially, if you incorporate in your abstract and conclusions that you are reaching different results in your analysis with those papers already published and using other type of methods (top-down).

Methods are acceptable well explained, though more details could have been given in order to deal with the survey data. This is important in your case in terms of replicating your analysis in other countries with similar databases.

Strengths and weaknesses of the methods are well stated in the discussion, though further explanations could have been given regarding the different definitions there are inter countries for smokers, former smokers and non-smokers.

Writing and organization is really well set in the paper, so I think that this has been well done by the authors! The paper is easy to follow by the reader! Tables and figures are ok!

Major Compulsory Revisions

This is a good and relevant paper to be published, though I think it is important to address first one issue. The only relevant problem I see with this paper is that the title and conclusions focuses in terms of smoking, however, methods and result do not do so! The paper explains methods and results in general in terms of this particular analysis on this database, but, I think, that you should focus the whole paper in the smoking data analysis, if you really want to introduce the smoking topic in the title. If you just want to analyze the database, not focusing on smoking that is fine, but probably will be other different papers with another aim and objectives!

So, I think that methods and results should be partly rewritten trying to focus in the smoking context. This should be sorted before publishing this paper, because it is difficult for the reader in terms to focus the attention in the results and establish connections among the different sections of the paper.
- Thank you for this remark. The aim of our work was to analyze the impact of smoking status on healthcare utilization, work absence and costs and to calculate excess costs of smokers compared to never smokers in a population-based survey.

- We understand the tables that we presented in the first version did not focus on the effects of smoking. Therefore, the comprehensive tables on regression results were shortened in order to strengthen the smoking focus. Full regression results can now be found in the online appendix. In addition, the discussion section was partly rewritten in order to strengthen the focus on smoking and to improve comparisons with similar studies. Finally, the title of the study was improved in order to include indirect cost and to clarify the cross-sectional character of the analysis.

- In the methods section, however, a detailed description of methods is necessary from our point of view. A comprehensive explanation of the data, on the handling of self-reported information and the costing approach as well as on statistical methods is given in order to document our proceedings.

**Minor Essential Revisions**

I will strongly recommend incorporating the definition for smokers, former smokers and non-smokers that you are considering in your paper. This is really important in terms of comparing your results across countries (especially, to know if you can do sensible comparisons or not!).

- A more detailed definition of the classification of smokers, occasional smokers, former-smokers and never smokers was added to the methods section, see p.4:
  “Participants were classified as current smokers if they smoked at least one cigarette per day at the time of the interview, as occasional smokers if they smoked usually less than one cigarette per day, as former smokers if they had smoked regularly or occasionally in the past and as never smokers if they had never smoked or less than 100 cigarettes in their lifetime.”

Extensive comparisons between results of this paper and results on papers using top-down approaches should be accrued in the discussion section.

- The structure of our discussion section was re-organized:
  Findings regarding utilization patterns of smokers and on costs were compared to similar international studies. The comparison with previous German top-down studies on the cost of smoking was extended; methodological differences between the approaches and their effects on results were described in more detail.
Reviewer's report 2

Title: The effect of smoking status on healthcare utilisation and costs: results from the population-based KORA F4 study
Version: 2 Date: 22 January 2013
Reviewer: Nadine Berndt

Reviewer's report:

This is a well-written and well-designed study. The paper's organization and quality meets the standards of similar manuscripts found in scientific journals. However, there are several points that need to be addressed. I'm certain all of my questions and comments can be revised without problems. I hope they are helpful and instructive, the paper concerns a good topic with significance to the costs of smoking in Europe and should be brought forth to disseminate the findings. Congratulations on completing the project!

Discretionary Revisions

1. Title: The title only concerns the effect of smoking on healthcare use and costs, however, the authors also looked at indirect costs (such as productivity losses). The title is now misleading and may be adjusted.

   - The title of the paper was reformulated in order to include indirect cost and to clarify the cross-sectional character of the analysis.
     We changed it to:
     “The association of smoking status with healthcare utilisation, productivity loss and resulting costs: results from the population-based KORA F4 study”

2. In the third paragraph of the introduction the authors state ‘the actual impact of smoking on costs of care can be focused on by estimating excess costs of smoking in a data set comprising current utilisation of individuals’. Please reformulate this sentence for enhanced understanding.

   - Sentence was reformulated for enhanced understanding, see p.4.
     Reformulation: “Alternatively, the actual economic impact of smoking can be calculated by estimating excess costs of smokers compared to never smokers in a data set comprising current utilisation of individuals.”

3. It is not clear from the introduction which perspective the authors used in their study while it seems that a societal perspective was used (since costs outside the healthcare sector were also measured). This information may be added.

   - societal perspective was added in introduction, see p.3

4. Paragraph 4, introduction. What were the a priori identified hypotheses of this trial? Lack of identified primary hypotheses lead to confusion whereas specifying these may enhance the quality of the paper (in the discussion the authors may then refer to the hypotheses).
- A predefined hypothesis was not included in the introduction as it was our primary aim to compare healthcare utilization and costs between different smoking groups, as stated in the last paragraph of the introduction section. Our proceeding combined estimations and testing of hypotheses. The implied hypothesis was that smoking status is not associated with healthcare utilization and costs.

5. Methods, under data and study design. Were smoking-related diseases not measured in participants (including cardiovascular diseases, respiratory diseases, and cancer)?

- In general, participants of KORA surveys are asked about a number of common diseases and run through a number of examinations.
- However, this information is not necessarily needed in an economic analysis according to the bottom-up approach which was used in this analysis. Distinguishing between smoking-related and non-smoking-related diseases is difficult as is attributing healthcare utilization a primary diagnosis, especially when only patient reports are available.

6. Paragraph 4, under direct costs (Methods). How did the authors deal with over-the-counter pharmaceuticals? Are those the so called non-pharmacy medications?

- In our analysis, self-medication which can be purchased outside of pharmacies was excluded. This comprises non-pharmacy medicines, dietary supplements, vitamins, as described on p.8. Other self-medication which is available only in pharmacies, but without prescription, was included in the analysis. The corresponding description was improved, see p.8. “Non-pharmacy medicines, dietary supplements, vitamins and non-pharmacy medicines were excluded.”

7. Results, regression analysis. In Table 3 the authors report ORs for all cofactors, and the 4 groups of smokers. However, only the results for the 4 smoking groups are described in the Results section. What is the additional benefit of presenting the ORs of the other factors? The Tables are relatively large and much information seems to be redundant. Consider shortening Table 3 (and Tables 2 and 4) by only presenting the results of the 4 smoking groups. These Tables could be easily shortened by presenting adjusted ORs for the smoking groups.

- Thank you for this advice. We agree with this remark and we decided to shorten all tables of regression analyses (tables 2,3,4) and focus on the estimates of the effect of smoking groups on utilization and costs. Detailed tables will be added to the online appendix for readers who are interested in the effects of cofactors.
- We hope that this proceeding also contributes to focusing the paper on the smoking aspects, as reviewer 1 suggested.

8. Tables 2-4. The deviance values and dispersion values are illustrated. Some explanation and elaboration might be included in the manuscript because many readers may be unfamiliar with these model-fit values.
- As tables 2-4 were reduced, information on deviance and dispersion moved to online appendix for interested-only readers.

9. Discussion. Some discussion may be incorporated about the fact that smokers may currently have higher costs than non-smokers, but non-smokers live longer and hence can incur more health costs at advanced ages.

- The fact that longitudinal studies are needed to investigate if higher annual healthcare costs of smokers and former smokers are outweighed by less lifetime-costs was mentioned as a limitation of our study in the discussion section with appropriate references, see p. 18

10. Discussion. The authors suggest that their findings are in line with other international studies on the costs of smoking and refer to several studies. In California, a study group has done quite a lot of research on the costs of smoking, but a reference to their work is lacking (see for example: Max, W. The Financial Impact of Smoking on Health-related Costs: A Review of the Literature. American Journal of Health Promotion. 2001, 15(5)).

- Thank you for this information. We included the review on the cost of smoking from Max et al. in our paper as it provides a good overview on similar studies. Further research of Max et al. focusses on costs of smoking in special subgroups, on the effects of secondhand smoke and on tobacco control programs which do not fit in our analysis.

11. Editing by a native speaker might be considered to correct minor misuse of terminology, prepositions, and grammar.

- We improved linguistic deficiencies throughout the manuscript by consulting a native speaker.

Minor Essential Revisions

1. In the first sentence of the introduction, tobacco smoking should not only be labelled as a health risk, but as a health risk behaviour.

- Terminology was improved, see p.4
  “Worldwide, tobacco smoking is seen as the most urgent health risk behaviour requiring prevention today [1].”

2. Methods. Years of education: 1011 should be adjusted to 10-11 years.

- Revised, see p.6

3. Throughout the manuscript the authors confuse the term "participants" with other terms (subjects, patients, individuals, etc). For example in the second and third paragraph under direct costs (Methods), the authors confuse the terms participants with users and patients. Please be consistent in the terminology.
- Terminology was harmonized throughout the manuscript in focusing on the term “participant”.

4. Table 1, footnote. The sentence seems to be incomplete. It should be added that those 3 subjects with missing data on school education were excluded from the analysis.

- Revised, see Table 1. Now reads: “a n=3 participants with missing information on school education. These subjects were excluded from the regression analysis”

Major Compulsory Revisions

1. Introduction, paragraph 1. The authors suggest that morbidity and mortality associated with smoking has financial consequences for healthcare systems and economies. Evidence for this statement is needed.

- Appropriate references for the burden on healthcare system and on economies was added, see p.4

2. Introduction, paragraph 3. Information about the smoking prevalence in Germany is lacking. A comparison with the financial burden of smoking in another (European) country should be added since the information about €17.4 billion to €33.6 billion otherwise might be misleading.

- We share your opinion and information on smoking prevalence in Germany was integrated, see p.4. As mentioned in the discussion section, smoking prevalence found in the KORA study is lower than national prevalence mainly because the KORA participants are older, see p.16.

- We did not aim at comparing cost estimates for different countries, as this make only sense if per-capita costs are calculated. Comparing costs of smoking in different countries would go beyond of the scope of our study as these studies are very heterogeneous, underlying data, methods and assumptions needs to be analyzed and costs need to be adjusted to purchasing power parities. Information about costs between €17.4 - €33.6 billion in Germany, which were shown in previous studies, corresponds to different base years (this information was added, see p.4).

3. Introduction, paragraph 4. While the selected bottom-up approach is appropriate and relevant, the introduction section needs to include an improved rationale (including references) for the choice of the bottom-up approach.

- Rational and advantages of bottom-up approach were included in the introduction and referred, see p.4f.

4. Methods, data and study design. Although the authors refer to previous studies, some additional information about the design, sampling method and data collection of the S4 and F4 study should be integrated. As such, information about inclusion criteria
of participants (if appropriate), and the way the baseline examination and follow-up measurement were conducted is lacking. Were these equally conducted?

- Additional information was added regarding the KORA study. There were no further inclusion/exclusion criteria for the KORA health surveys, see p.6f.
- Detailed healthcare utilization was solely documented in the F4 survey, therefore no longitudinal analysis was possible.

5. Methods, data and study design. In other countries than Germany, the education system is different. Please refer to primary, secondary and post-secondary education. Years of education are redundant.

- Due to differences in educational systems and special customs in the German educational system, we would like to keep the terms “basis, secondary, higher education”. In order to enable comparisons with previous/future studies, we would like to report the years of education in addition.

6. Methods, data and study design. Please indicate how smoking status was measured in participants and how it was defined. How much did participants need to have smoked to be treated as a current, occasional former, or never smokers?

- A more detailed definition of the classification of smokers, occasional smokers, former-smokers and never smokers was added to the methods section, see p.6, as follows:
  “Participants were classified as current smokers if they smoked at least one cigarette per day at the time of the interview, as occasional smokers if they smoked usually less than one cigarette per day, as former smokers if they had smoked regularly or occasionally in the past and as never smokers if they had never smoked or less than 100 cigarettes in their lifetime. Smoking status in F4 was compared with previous S4 information, and nine participants were excluded due to missing or implausible information on smoking status.”

7. Methods, data and study design. Distinctions are made between low and risky alcohol consumption, and active versus inactive participants. It is unclear if these distinctions are based upon some national guidelines. If so, please add the relevant references.

- Categories for risky alcohol consumption and for physical activity are based on WHO recommendations. An appropriate reference was added, see p.6.

8. Methods, direct costs. In the first paragraph more description of the measurement of the costs is needed. Which index year was used, was it 2008? From which year were the national unit costs derived by the AG MEG? Were these unit costs inflated to the year 2008? The study period was from 2006 to 2008, and the follow-up period was longer than 1 year. How were costs and smoking status discounted? Please specify.

- All healthcare utilization was valued with prices of the year 2008, as described on p.7.
- German unit costs were updated to 2008, which is the base year of our study. Krauth et al. (2005) calculated German unit costs for different healthcare
categories with different base years (e.g. 1999 for physician visits, 2000 for hospital stays). This information was added to the manuscript, see p.7f.

- Discounting within the F4 study was not necessary since healthcare utilization was assessed for one year only and costs were calculated for the base year of our study.

9. In the Methods under indirect costs it is stated that the number of days of working absence were restricted to 213. Why 213? In the second paragraph the Friction cost method is mentioned. This approach was originally developed by a group of Dutch economists (see for example Koopmanschap et al., 2005). This reference is lacking and should be inserted.

- According to the German Institute for Employment Research, the average maximum number of working days in the year 2008 was 213 days (366 days less weekends and holidays). The explanation was improved in the manuscript, see p.8.
  “If participants stated a greater number of days of absence from work than the maximum number of 213 working days in 2008, their days of absenteeism were restricted to 213 (n=6).”

- Koopmanschap et al. Journal of Health Economics, 2005 was added, see p.9, reference [38].

10. Methods, statistical analysis. How did the authors deal with missing data and outliers in costs (if applicable)? It seems that participants with missing data were excluded from the analyses, but this needs to be specified.

- As described in the methods section, 9 of 3080 participants of the F4 survey had to be excluded due to implausible information on their smoking status, see p.6.

- Except three observations with missing information on school education, there were no missing values in explanatory variables (Age, sex, physical activity and alcohol consumption). These three observations were excluded from the regression analyses as stated in the explanation of tables and in the section on statistical methods on p.10.

- Regarding healthcare utilization, there were some missing values regarding the frequency of utilization. The handling of these missing is described on p.5.
  E.g. there were 7 participants who stated that they had a physician visit, but did not state their number of visits. According to a conservative approach, one visit was imputed. In a sensitivity analysis, the mean number of physician visits was imputed instead.

11. Methods, statistical analysis. The way the regression analysis were conducted should be better described. Please clearly explain which approach was used. Was it in one or two steps?

As regards Tables 3 and 4, the Odds Ratios of the 4 smoking groups are of real interest, which seem to have been adjusted for the other co-factors. The other information in the Tables seems redundant. Please clarify.
- Statistical methods are described on p. 9f.
- Healthcare utilization was analyzed in two steps, because a number of observations did not use all healthcare categories: first, odds ratios for healthcare utilization (yes/no) were calculated. Second, the frequencies of healthcare utilization were analyzed.
- Regarding costs, there was a one-step procedure as only few observations in the survey had zero costs.
- Tables 2-4 were shortened and restricted to the estimates regarding smoking status. Comprehensive results of regression analyses moved to the online appendix.
- All regression analyses were adjusted for age, sex, school education, alcohol consumption and physical activity.
- An appropriate sentence on the two-step approach regarding utilization was added, see p.9.
  
  "The effect of smoking status on healthcare utilisation and work absenteeism was analysed in a two-step approach." 

12. Results, Table 1, unadjusted analyses. In describing the characteristics of the study sample, please indicate if the 4 smoking groups were comparable in their characteristics. Regarding the proportions, it seems that current and never smokers might differ on some variables (sex, alcohol consumption).

- p-values of appropriate tests for the comparison of the smoking groups were added to table 1.
- An additional sentence on group differences in confounding variables was added, see p.11.
  
  "Groups differ significantly regarding sex (p<0.0001), age (p<0.0001), and consequently in alcohol consumption (p<0.0001) and physical activity (p<0.01)."

13. An additional sensitivity analysis might be beneficial especially because of the uncertainty in costs and smoking outcomes that resulted from high risks of recall bias and extrapolation of costs to 12 months. Did the authors consider a sensitivity analysis in which all participants of whom the smoking status could not be specified in F4 /lost to follow-up (28%) are regarded as smokers?

- Using all participants which were lost to follow up between the S4 and the F4 study for an additional sensitivity analysis is not possible, because in addition to missing information on actual smoking status in F4, there is no information on the utilization of healthcare services in the follow-up. Only F4 data was used for this analysis. Therefore costs of lost-to-follow-up persons cannot be calculated for F4. Furthermore, smoking status was defined according to F4 information.
14. Discussion. The comparison to other international research is rather general. The authors mention that their findings are in line with other international studies that have shown increased costs due to smoking. Could the authors give a specific example of an international study that has shown similar findings? Did these studies use a bottom-up approach as well?

- Regarding our findings on healthcare utilization of smoking groups, two additional comparisons with similar bottom-up studies were included, see p.14.
  “Similar to a health survey from the US [8], we found an increased risk of inpatient visits and an increased number of physician visits in former smokers. Our findings that current smokers showed a lower probability of physician treatments, but a higher number of treatments if this group used physician treatments at least once, is comparable to a recent study which found a decreased likelihood of current smokers to use primary care services but slightly increased costs [43].”

- To our knowledge, there is no similar international study which compares results of top-down/bottom-up approaches on costs of smoking.

15. Discussion. The structure of the discussion seems to be poorly organized, since the authors first give a very short summary of their findings, and then mention their limitations very broadly. I would consider moving paragraphs 11-15 to the beginning of the discussion, this information might be better placed before the limitations. Also, all limitations should be in one section, whereas now they can also be found in various paragraphs (such as paragraph 14). Moreover, the discussion of the main findings is relatively short in comparison to the discussion of the limitations. This needs to be balanced better.

- Thank you for this helpful remark. Therefore the structure of our discussion section was fundamentally re-organized:

  o After a short summary of our findings, we compare our findings on utilization patterns with findings in similar international population-based studies. This part was extended. Afterwards, the influence of the time of quitting in the group of former smokers is discussed and compared to other studies.

  o In the next part, there is a comparison with existing studies on the cost of smoking in Germany. As these previous studies rely on top-down approaches, advantages and disadvantages of top-down and bottom-up studies are given. This part was re-elaborated. A detailed comparison of our results with top-down results is made. Potential reasons for differences in results are discussed.

  o We moved the limitations part to the end of the discussion section. Limitations of our study are discussed in detail as there are a number of sources of uncertainty resulting out of the use of self-reported data of survey participants. Specifying these limitations should enable comparisons with similar bottom-up studies and give guidance for future research questions.
16. Discussion. Please compare the prevalence of smoking as found in your study to the prevalence of smoking in Germany, since this information is now completely lacking. Is smoking prevalence expected to decrease or increase in the future (and what is the expected economic burden)?

- German smoking prevalence was added in the introduction, see p.4. “In Germany, smoking is still prevalent despite a reduction in recent years: 30% of the population aged 18 and older are smokers, 26% former smokers while 44% have never smoked [7].”

As mentioned in the discussion section, the smoking prevalence found in this KORA survey is lower than national average because of higher mean age of KORA participants. For the extrapolation of our results to Germany, national prevalence rates were used, see p. 16.

- According to the German Robert-Koch-Institut, smoking prevalence in Germany is now slightly decreasing. This information was added, see p.4. (it can be expected that this leads to decreasing economic burden, but this cannot be analyzed using our cross-sectional dataset).

17. Discussion. Some costs were measured over the past week or the past 3 months, whereas others were assessed over the past 12 months. As a result, some costs needed to be extrapolated to 12 months and others did not. Recall bias and extrapolation may have led to uncertainty in the estimation of costs. Please give some rationale whether and why these were (un)likely to have affected the validity of the results.

- An additional reference (Seidl et al. 2012) was added showing that cost data can be collected efficiently by reducing the frequency of data collection. Extrapolation of resource categories which were measured for 3 months was shown to be appropriate.

- If nevertheless recall bias may have occurred in the KORA survey, this should only influence the estimated average costs for all participants, not the differences between the smoking groups. This point was added, see p.17. “Nevertheless, recall error may have occurred, but it is unlikely to have affected the validity of our results because this may not have influenced the differences between the smoking groups [46].”

18. Discussion. In the last paragraph before the conclusion, it is stated that another German study using a top-down approach found much less costs per current smoker. Was this difference only due to the nature of the study (top-down vs. bottom-up) or are there also other differences that explain the discrepancy in study outcomes?

- The fact that top-down studies find lower costs per smokers than bottom-up studies is due to methodological differences as top-down studies cannot consider the entire spectrum of smoking-related diseases

- An additional paragraph on the differences of top-down and bottom-up studies was added in the discussion section in order to facilitate the explanation of differences in results, see p.15 and better explanation was added on p.16. “To date, only a few studies have examined the economic burden of cigarette smoking in Germany [19-22]. Using a top-down approach, these studies
identified direct and indirect costs attributable to smoking of €17.4 billion for the year 1993 [21] and €21 billion for the year 2003 [20]. As this approach uses the concept of smoking-attributable fractions for mortality and morbidity known to be caused by smoking, health conditions where smoking may be one of several contribution factors are neglected. Furthermore these previous top-down studies used attributable mortality risks for attributing morbidity. Mortality risks may differ from morbidity risks and from healthcare utilizations probabilities. In addition, in focussing on mortality risks this method solely considers smoking-related fatal diseases and neglects non-fatal health consequences of smoking like e.g. osteoporosis or eye diseases like cataract and glaucoma. Therefore is approach is known to downward-bias cost estimates [26].

Compared to top-down approaches, calculating excess costs based on subject-level data has the advantage of considering the entire spectrum of disease consequences associated with smoking. In addition, the bottom-up methodology used in this study provides better adjustment for the actual impact of smoking on health conditions and for population characteristics as it considers other differences in smokers and non-smokers regarding education and other risky behaviours besides smoking.”

19. In the end of their conclusion the authors refer to WHO Framework Convention on Tobacco Control. Can the authors give a specific implication on how to decrease the economic burden of smoking by realising this Framework?

- Revised, an additional explanation was added, see p.14

“…for example in realising the WHO Framework Convention on Tobacco Control [49] which suggests measures to reduce tobacco demand and therefore prevents smoking and its negative economic consequences.”
Reviewer’s report 3

Title: The effect of smoking status on healthcare utilisation and costs: results from the population-based KORA F4 study
Version: 2 Date: 12 February 2013
Reviewer: Dennis Petrie

Reviewer’s report:

Review of “The effect of smoking status on healthcare utilisation and costs: results from the population-based KORA F4 study” for BMC Health Services Research.

General Overview

The paper makes use of self-reported data on smoking status and healthcare utilisation in Germany to explore the association between different smoking states and their healthcare costs while controlling for a number of other factors. They present a number of interesting findings regarding how types of healthcare utilisation and indirect costs related to productivity losses differ among the classes of smokers. They also find that the differences in costs between never smokers to current and former smokers suggest that the healthcare costs relating to smoking may have previously been underestimated. In general the methods seem appropriate and the paper presents useful information for other researchers in this field.

Discretionary Revisions

1. Title: I think the word “effect” in the title is slightly misleading as the study is a cross-sectional study which looks at the association or relationship between smoking status and healthcare utilisation and costs while trying to control for other factors (i.e. it’s hard to conclude that becoming a former smoker would increase your healthcare utilisation and costs compared to if you had kept being a current smoker).

   - The title of the paper was reformulated in order to include indirect cost and to clarify the cross-sectional character of the analysis.
   - Now reads: “The association of smoking status with healthcare utilisation, productivity loss and resulting costs: results from the population-based KORA F4 study”

2. Data and Study Design: I think it could be made clearer about whether the controlling factors relate to those reported in KORA S4 or F4? And in particular the smoking variable?

   - Revised, see p.6
   - All variables used in this analysis originate from the F4 survey.
   - Only for validating the self-reported information on smoking status of F4 participants, information on smoking status from the S4 survey was used in
order to compare the information. Nine observations had to be excluded from
the analysis because of missing information on smoking status in F4 or
implausible information on smoking status when comparing S4 and F4
information.

- Unfortunately, a longitudinal analysis was not possible because questions on
healthcare utilization were not fully comparable between the KORA S4 study
and its follow-up F4, which was used here.

3. Utilisations of medical services: For a non-German I would have liked a
brief overview of how the German health system works – in particular
whether there are out-of-pocket costs for any healthcare utilisation
mentioned or whether these are full subsidised by the government? This
would have allowed me to put the results in a wider context.

- Germany has a universal multi-payer health care system with two main types
of health insurance: statutory health insurance (~85% of population) and
private health insurance (~11% of population). In the statutory system,
providers are paid directly by health plans except for a limited patient co-
payment, which is capped at 1%–2% of gross income. The system utilizes a
pay-as-you-go financing system based on premiums, with no capital reserves.
Access to private health plans is restricted to higher-income individuals.
Premiums in the private system are based on individual health risks. In the
private system, members pay providers directly and are reimbursed by their
health plans. Private health plans hold capital reserves.
The German system is characterized by self-governance, in contrast to
centrally directed systems such as the National Health System in the UK. (see
Porter M, Guth C. The German Health Care System: Overview and Historical
Development. In: Porter M, Guth C. Redefining German Health Care Moving
to a Value-Based System. 2012)

- For our analysis, all costs were calculated from a societal perspective.
Therefore, special characteristics of the German healthcare system, like out-
of-pocket costs, are not relevant, because by using German unit costs
consumption of resources was priced regardless who carries the costs.

4. Statistical Analysis: The use of the negative binomial regression for “users
only” seems slightly strange given that the negative binomial also supports
zero use even though by construction the “users” will only have non-zero
usage? Some clarification here would be welcomed about why a zero-
truncated model was not used or why the negative binomial is more
appropriate in this case?

- You are right in that the negative binomial also supports zero-valued
observations. However, there are excess zeros in most of our healthcare
categories (e.g. for alternative practitioners, where 2,850 out of 3,068
participants did not report health care use). In such situations, the amount of
zeros is usually much higher than expected under the count process assumed
for the remaining observations with non-zero use. This is why we preferred to
model zero counts and non-zero counts separately.
5. **Statistical Analysis**: I think you should state that no significant non-linear relationships and interactions were observed. Also you should mention or reference the variable selection methods you applied to come to this conclusion. I think it would be worth the last statement in this section coming before this as it puts into context why no interaction terms were considered (i.e. because I’m guessing they weren’t significant at the 5% level).

- Additional information on variable selection methods in SAS was added, see p.10
  “Non-linear relationships of variables were checked as well as possible interactions by using variable selection methods (PROC GLMSELECT with stepwise selection method), but no significant non-linear relationships and interactions were observed.”

6. **Sensitivity analysis**: “Varying the costs attributed to subjects with zero costs in the regressions” – I think you should be clear about the lowest value and the highest value you tested which didn’t impact on the conclusions – at some stage it might start making a difference (also I can’t imagine that it wouldn’t impact on the coefficients at all? - currently it is a very strong statement)

- Details on the amount of costs which was attributed to participants with zero costs for the regression analysis in the sensitivity analysis was included, see p.13. We decided to vary the amount between €0.5 to €5 as the participants with the lowest non-zero costs in the study sample caused costs of €7.
  “Also, varying the amount of costs attributed to participants subjects with zero costs in the regression analysis from €1 to €0.5 or €5 affected neither the coefficients nor their significance.”

7. **Discussion**: Some comment on the longitudinal aspects of these risk behaviours (smoking, alcohol consumption and physical activity) would be helpful – these also could have also changed in response to health shocks or been selected originally due to underlying levels of health. This also ties in with the finding that high risk alcohol consumption is associated with lower direct medical costs (also for alcohol often the abstainers are treated as a separate group for a number of reasons – I wonder whether they are increasing the costs for the low risk group?).

- In general, the aim of our approach is to compare the costs of smokers and a hypothetical group of “nonsmoking smokers” – people who have the same demographics and risk factors as those of smokers except that they have never smoked. You’re right that also other risk behaviors (physical activity, alcohol consumption) could have changed as a result of health shocks. It is a limitation of our cross-sectional study and this point was entered to the limitations section, see p.18.
  “Nevertheless, the levels of physical activity and alcohol consumption could
also be the result of underlying health conditions which cannot be analysed in cross-sectional data.”

- Regarding alcohol consumption: we grouped alcohol consumption in 2 levels (low risk – high risk consumption) according to former WHO recommendations (reference was added). Treating abstainers as a separate group would be more appropriate when the effect of alcohol consumption on costs is analyzed.

8. **Discussion:** The comment about selection bias should also refer to self-selection into these smoking states.

- Our argumentation on selection bias on p.17 also covers the possibility of self-selection of participants.

9. **Discussion:** I found that a number of the more interesting comparisons were simply stated in the discussion section and not included in the results (comparisons among when the former smokers quit and those who quit for medical reasons versus those who quit to prevent future disease) – it would have been nice to at least make these results available to others as I found this to be the most interesting part of the paper and I think these results tell us more about the potential causal story relating to smoking status?

- Thank you for this advice. We decided to report on additional subsample analysis of former smokers earlier in the results section, see p.12f., and then discuss findings in the discussion section.

“Analysis of a subsample of former smokers showed that participants who quitted smoking in the last 12 months caused 2.37 (p<0.0005) times higher total costs than former smokers who quitted more than 12 months ago. Further subsample analysis in 791 former smokers showed that participants who quitted because of medical conditions caused significantly higher costs (92%) than former smoking participants who did not quit because of this reason. Former smokers who quitted in order to prevent future diseases showed only 63% of costs of participants for whom prevention was not an issue. Other reasons like financial aspects, pregnancy or fear of lung cancer had no significant influence on total costs in this subsample.”

10. **Conclusion:** A broader comment on the usefulness of a longitudinal analysis might be a good suggestion for future research within the paper – in particular a more interesting question is what health care costs could be saved if we could encourage current smokers to become former smokers (or if we could stop smokers starting in the first place). But obviously this would require more detailed longitudinal data than you currently have available.

- The remark that our analysis is only an estimation of annual cost and that longitudinal studies are needed in order to investigate dose-effect relations and the influence of the circumstances of quitting on costs was improved, see p.19.

“Although further research is needed to examine dose-effect relations of
smoking, the timing of quitting on societal costs and results from longitudinal studies and further long-term effects of smoking, policy makers should strengthen their efforts towards prevention…”