Author’s response to reviews

Title: Rhinosinusitis in morbidity registrations in Dutch General Practice: A retrospective case-control study

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Author’s response to reviews: see over
Dear Dr. Tsiligianni,

With reference to your letter with revision instructions of 4th of June 2015 we would like to thank you for reviewing our manuscript entitled “Rhinosinusitis in morbidity registrations in Dutch General Practice: A retrospective case-control study”. The comments were very useful to improve the quality of our manuscript. We agree on most comments and would like to respond to the reviewer’s comments by this letter and by revision of our manuscript. The following changes are made:

Reviewer Jaime Sousa:

1. **Comment**: It is unclear if the protocol was reviewed and approved by an ethical board
   
   **Response**: This retrospective case-control study did not need approval of an ethical board since the anonymous participants in the already existing database were not submitted to investigations or actions as part of this study. We added this to the Methods section.

2. **Comment**: The authors mention that in the CMR there is a list of codes based on the E-list and the ICHPPC-2-defined criteria. In the CMR, separate codes for ARS and CRS exist. This needs clarification as the ICHPPC-2-defined uses the same code for ARS and CRS (position 134, Code 461 - Sinusitis, acute and chronic). How is this detailed in the clinical record?
   
   **Response**: In the CMR a list of codes based on the E-list compatible with the ICHPPC-2-defined criteria is used (instead of E-list and ICHPPC-2-defined). This sentence was changed in the manuscript. In the E-list, separate codes do exist. As a result of an agreement between the participating GPs, the code for CRS is not used.

3. **Comment**: The statement “The prevalence of ARS and CRS was 5197 and 65 respectively.” Should be clarified. Prevalence should be expressed in per cent or per mil
   
   **Response**: Prevalence is now expressed in per mil.

4. **Comment**: These statements should be reviewed as they seem contradictory: page 7, line 140-142 - “In the TP no difference is made between ARS and CRS. However, the length of the episodes of care is registered and we used this information to
discriminate between ARS and CRS.” Page 9, line 176-177- “Reliable
determination of the length of episodes was not possible in the TP data, so no
discrimination between ARS and CRS could be made”.
Response: Indeed this seems contradictory. We clarified this by adding “tried
to” use this information on page 7. We added “Reliable determination of the
length of episodes was not possible in the TP data, despite the code for the
end of an episode. Because an episode can end in between two visits to the
GP, the exact end of an episode remains unknown.” to the results section on
page 9.

5. Comment: The authors should explain in the methods section why they
couldn’t access information about the medication used.
Response: The sentence: “Only the kind of intervention was coded, for
eexample prescription of medication, but not exactly which medication was
prescribed.” Was added to the methods section

6. Comment: In page 12, line 248, the authors state “Antibiotics are still
prescribed quite often for this indication”, but as mentioned before, there is no
data about antibiotic prescribing.
Response: A reference to literature was added.

7. Comment: The section dealing with external comparison of the results, could
strengthened by including a broader discussion of the general limitations of
using current clinical data for epidemiological surveys after page 13, line 270.
A note should be added about a study design that could overcome these
limitations.
Response: Some additional issues are added to the discussion:
- For the diagnosis we depend on the GP’s assessment, we are not sure
  that inclusion criteria are strictly followed.
- It was found that questionnaire-based and clinical based CRS show
  moderate correlation, GPs have no access to nasendoscopy and/or CT.
- Ideally registries with clear inclusion criteria for rhinosinusitis, using the
  unambiguous definitions of rhinosinusitis as defined in EPOS, should be
  used in a study like this. Information on interventions should be more
  precise, giving more insight in the medicaments prescribed and the
diagnostic radiology that is applied for.

8. Comment: The sentence “Decongestants, antibiotics, analgesics, nasal
steroids and antihistamines are some of the commonly prescribed treatments”
in page 15, line 516-17 seems inappropriate, as there is no data from the
study supporting the statement
Response: A reference to literature was added and a sentence stating that
prescriptions of these medicaments cannot be confirmed by our study was
added.

9. Comment: Conclusion: This section should be rewritten to also include the
most relevant positive conclusions of the study.
Response: The most relevant positive conclusions were added to the
conclusion: Rhinosinusitis is a common diagnosis in general practice. Based
on two morbidity registrations in general practice, the diagnosis can be related
to several other diagnoses as allergic rhinitis and nasal polyps. Medication is
prescribed in 91% of the cases and almost 8% is sent for diagnostic radiology.
Reviewer Herbert Riechelmann:

10. **Comment**: Based on a recurrence code, the authors can distinguish between incidence and prevalence (p6, last para).
   **Response**: When the code for an already existing episode of rhinosinusitis was used, that (same) episode was not included again for calculation of the incidence of rhinosinusitis. This explanation was added to the manuscript.

11. **Comment**: What is “literature” (p7, last para)?
   **Response**: The references for “literature” moved directly behind the word literature to clarify this.

12. **Comment**: Are nasal polyps a comorbid condition of rhinosinusitis (p7, last para)?
   **Response**: Indeed it is unclear whether nasal polyps and rhinosinusitis are one disease or two different entities. According to the codes in the registrations they are. A sentence clarifying this is added to the manuscript.

13. **Comment**: In the statistical analysis part, the denominators of the odds should be mentioned. The authors arbitrarily choose an OR of more than 3 or an lower 95% CI bound to attest relevance. What is the rationale for this? (p8, 2nd para)
   **Response**: The denominators of the odds were added to the methods: (odds of comorbidity in rhinosinusitis population/odds of comorbidity in population without rhinosinusitis) Statistically an odds ratio above 1.0 and a 95% confidence interval not including 0 is a significant association, but maybe not clinically relevant, therefore we (indeed arbitrary) chose an odds ratio of more than 3.0 in combination with the lower limit of the 95% confidence interval above 2·0 to be a relevant association.

14. **Comment**: If the database does not allow to differentiate between ARS and CRS, it might be wise not to try to differentiate, but use the term RS.
   **Response**: Because we think that it is important to differentiate between ARS and CRS, as they may be two different diseases, we want to make a point by using both terms.

15. **Comment**: If no data on prescribed treatments are available, it might be wise not to speculate about this (p 12, 3rd para) but refer to data published in a previous publication
   **Response**: A reference to literature was added.

16. **Comment**: consider unambiguous instead of uni-interpretable
   **Response**: We changed uni-interpretable to unambiguous

We would like to submit our revised manuscript and would like to ask you to consider publication in BMC Family Practice.
If you have any further questions, please do not hesitate to contact us.

On behalf of my co-authors,
Sincerely,

Ruth Hoffmans