Reviewer’s report

Title: Prevalence and clinical associations of wheezes and crackles in the general population. The Tromsø Study

Version: 0 Date: 06 May 2019

Reviewer: Ramesh Kurukulaaratchy

Reviewer’s report:

General Comments:

This paper reports the prevalence of auscultatory adventitial lung sounds in a sample of mid to older age adults drawn from a whole population sample in Norway. As such it provides some interesting insight into the general occurrence of physical signs usually observed in relation to clinical disease. Methodology appears generally reasonable but some areas of comment are highlighted below. Analysis is generally appropriate. The findings are intuitive and of moderate novelty. The conclusion that such abnormal physical signs are variously associated with increasing age, clinical disease, smoking status, female sex, oxygen saturations and lung function are logical in the population being studied. That abnormal physical signs are not uncommon in this group is a potential reminder to consider the presence of subclinical disease in otherwise apparently healthy individuals. This point certainly merits emphasis whilst caution should be exercised in overstating that these signs are occurring in healthy individuals - they are potentially simply "apparently healthy" or "under-diagnosed". Some important conditions seem to be missing from those being documented in the study; for instance interstitial (fibrotic) lung disease and bronchiectasis could both cause crackles. That could underestimate the association of some auscultatory signs with clinical diseases that might be expected to be more prevalent in older age group. That points needs recognition and discussion.

Overall the paper can be a useful addition to the literature as a reference work but several clarifications, acknowledgment of additional limitations and specific revisions are recommended. In addition careful proof reading to improve grammar and clarity of message would be helpful. Specific comments below.

Specific Comments:

1. Abstract/ Background/ P.2, Line 4; It is more appropriate to state "apparently healthy adults".

2. Abstract/ Conclusions/P.2, Line 20; It is more appropriate to state "over a quarter" rather than "nearly 1/3" - 28% is closer to 25% than 33%.

3. Background/ P.3, Lines 6-8. Interstitial (fibrotic) lung disease and bronchiectasis should be added to the list of conditions described.
4. Background/ P.3, Lines 8-10. This sentence does not convey a clear message and needs to be rephrased.

5. Background/ P.3, Line 11. This sentence could be made clearer by deleting "of ALS".

6. Background/ P.3, Line 13. It is more appropriate to state "apparently healthy adults".

7. Methods/ P.4, Line 2. Some outline of the purpose/ nature of the Tromso Study is required to set the present paper in context. A brief outline of methodology for that study would be appropriate and help inform the reader. That should be referenced. Please add.

8. Methods/ P.4, Line 6. It should say "were" not "where".

9. Methods/ P.4, Line 13. Were interstitial lung disease and bronchiectasis asked about in the questionnaire? If so that should be mentioned here. As a linked point the questionnaire used could be made available (English version) in the online supplementary section.

10. Methods/ P.4, Line 23. Please state whether lung function was pre or post-bronchodilator as that is essential for correct interpretation of results.

11. Methods/ P.6, Line 1. It is mentioned that 2 observers independently listened to all the recordings but then lists 4 names which is confusing. Is it that JCA listened to all recordings and one of either RE, AD, CJ were the 2nd observer? This sentence could be made clearer to aid understanding.

12. Methods/ P.6, Lines 14-15. Were these junior and senior observers the same as JCA, RE, AD and CJ or different? Please clarify.

13. Statistics/ P.7, Line 22. Is there a justification for taking p-value of <0.05 for selecting parameters for entry into the multivariate logistic regression when many researchers would use a less conservative p-value (eg <0.1 or even <0.2) to identify them?

14. Results/ P.8, Line 8-9. The studied population in this paper is a small proportion of the Tromso 7 study population. There are a couple of clarifications needed here. Firstly that the Tromso 7 population is representative of the general Norwegian population. Secondly that the subgroup presented in this paper is representative of the main Tromso 7 population. It should be possible presumably for the authors to present some data on demographics of those in the main Tromso 7 group compared to those in this subgroup? That could be placed in the supplementary material but referred to in the text.

15. Results/P.8, Line 11 & P.19. Differences in a series of descriptive parameters are presented stratified by sex in Table 1. Looking at the values presumably none of the differences are statistically significant. If so it would be useful to mention that in the associated text on page 8.
16. Results/ P.9, Line 1. There seems to be a discrepancy between the number included in the analysis reported here (n =262) and that reported in Line 5 (n =1131). I presume there is a logical explanation but it is not clear from the paper. Please clarify.

17. Results/ P.9, Line 6-7 & P.20. A few comments here. The text on page 9 doesn't clearly summarise the findings in Table 2. Specifically it should summarise what comparisons were significantly different as there appear to be several highlighted in the table. Also, with regards to the table it states that the p-values relate to "as compared to absence of characteristic". This needs to be made clearer. Was "Normal" used as a standard reference for comparison of each auscultatory status? Or is the comparison different? Looking at the p-values presented it doesn't seem that "Normal" was used as a standard reference for comparison eg Age≥ 65 years "both crackles & wheeze" = 4.4% and "Normal" = 66.4% but no significant p-values seem to be annotated. Again I presume there is a logical explanation but both in the text on page 9 and table 2 footnote there needs to be a clearer description of the comparison being presented.

18. Discussion/ P.10, Line 23. This should more appropriately read "not always related to clinically diagnosed disease".

19. Discussion/ P.12, Line 18. The omission of interstitial lung disease and bronchiectasis form the conditions at present defined in the paper is a significant one. Either that data should be presented if available or this should be noted as a limitation in this section of the Discussion. Both conditions would be expected to show an incident rise with advancing age and be associated with crackles on auscultation. It may therefore be that a proportion of subjects presently defined as healthy in this study actually had such disease.

20. Discussion/P.13, Line 11. The conclusions reported here are different to those reported in the abstract. From the manner in which the data are presented it isn't clear that the findings support the conclusion of not being concerned about wheeze or crackle in a single location. Also local obstruction eg inhaled foreign body or tumour could, for instance, cause localised wheeze and be concerning. That abnormal physical signs are not uncommon in this group is a potential reminder to consider the presence of subclinical disease in otherwise apparently healthy individuals. This certainly merits emphasis in the conclusion whilst caution should be exercised in overstating that these signs are occurring in healthy individuals - they are potentially simply "apparently healthy" or "under-diagnosed".

Please modify the conclusions here and align to those presented in the abstract.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

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