**Reviewer’s report**

**Title:** Screening of noise-induced hearing loss (NIHL)-associated SNPs and the assessment of its genetic susceptibility

**Version:** 0  **Date:** 03 Jan 2019

**Reviewer:** Ann-Christin Johnson

**Reviewer’s report:**

This is a very interesting paper with the aim to create genetic risk evaluation and prediction for NIHL among workers. The approach is ambitious and well preformed.

However, some questions needs to be addressed and the results also have ethical considerations that have to be taken, if this kind of screening should be made general.

Below please find my comments and questions.

**Abstract**

1. It needs to be clarified that it was 476 subjects with NIHL and 476 controls (if that was the case- see further below)

**Introduction**

2. Line 16; the National Institute…

3. Line 23; exposure, other risk factors and genetic risk factors. Com; Not only genetics influence the level of NIHL also other exposures like solvents, medication and vibration as well as life style factors and different diseases can influence NIHL.

4. Line 42, study populations were generally small ADD references to this

5. From Line 45 and forward; the end of the introduction is more a description of methods and results and should not be here. This part needs to be more general and end with WHY you did the study NOT how.

**Methods**

6. 2.1 - Line 35 and Figure 1; it is unclear what is meant by epidemiological examination??
7. 2.2 - Line 9-11. What does gender mean here? More detail is needed about how controls were selected.

8. 2.3 - Line 48 More detail of this cohort is needed. How many in total etc… Line 1-3; The same SNPs??, which were genotyped in XXX? of the subjects in the follow-up group. Com; Were all SNPs tested of which in all subjects or some??

9. 2.4 - Line 38-48 More details is needed about HOW the GRS was constructed preferably with an example for readers not familiar with the method. Especially how the SNPs that decreased the risk for NIHL were treated in this respect???

Results

10. 3.1 - Line 21 CHANGE TO no statistical significant difference between NIHL subjects and controls regarding smoking….noise intensities (P > 0.05)

11. 3.1 Second page - Line 21-23 This sentence belong to the Method section see comment 9 above.

12. 3.2 I like your figures they are clear and explanatory.

13. 3.3 second page - Line 1 and Table 3. The heading of the Table is wrong as it refers to the cohort study

14. 3.3 second page - Line 21 Divide Table 3 into two tables as the GRS results are of different character. Com; Were the GRS in the follow-up subjects based on the same SNPs as in the cohort study, even if the associations were not the same???

Discussion

15. Line 25; References needed

16. Second Page Line 23-30; This line of discussion should be more elaborated. Which ethical considerations has to be taken if this kind of screening should take place? Should workers with certain SNPs not be allowed to have certain jobs? This is not an easy question and the associations you found are interesting but by no means certain???. More studies is needed before a general screening can be suggested as prevention against NIHL!

17. Second Page Line 33; What did your earlier investigation show?

18. Second Page Line 38 and following. Discussion about the potassium channel genes are interesting and could be more elaborated and clearer if the results of the cited studies were mentioned briefly.
19. Third Page Line 16 Suggestion NIHL after noise exposure based on multiple SNP loci. One of the strengths of the study is that our preliminary established NHL risk prediction model using 14 SNPs to screen for High risk NIHL was partly validated in the follow-up study cohort using NIHL incidence over a 5 year period. However the sample size in the prospective cohort was relatively small and the follow-up time was relatively short, thus false negative results may exist. Further studies using both men and women as well as a larger sample size should be performed to validate the results.

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**Quality of written English**
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