

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Hemoglobin A1c and Hearing Impairment: longitudinal analysis using a large occupational health check-up data of Japan
AUTHORS	Nagahama, Satsue; Kashino, Ikuko; Hu, Huanhuan; Nanri, Akiko; Kurotani, Kayo; Kuwahara, Keisuke; Dan, Masashi; Michikawa, Takehiro; Akter, Shamima; Mizoue, Tetsuya; Murakami, Yoshitaka; Nishiwaki, Yuji

VERSION 1 – REVIEW

REVIEWER	Alessandra Samelli University of Sao Paulo
REVIEW RETURNED	13-Apr-2018

GENERAL COMMENTS	The manuscript is well written and the subject matter is current and important. The sample used is huge and this is a great potential of the study. The methodology is well described. The results and discussion are well described. However, there is a serious problem in the study. There is no mention of noise exposure and this aspect, when it comes to workers, can not be considered. Exposure to noise in adults can have important consequences for hearing. Exposure to noise associated with other risk factors such as metabolic diseases, smoking, alcohol consumption, among others, may potentiate hearing loss, since all these agents cause oxidative stress, which has negative consequences for hearing (see Falasca et al. al, 2017 - Noise Induced Hearing Loss: The Role of Oxidative Stress). Therefore, this question must be considered and, if there is no possibility of including the analysis that considers exposure to noise, at least a much more detailed discussion on these aspects should be made.
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REVIEWER	Joseph Wasson East Kent Hospitals University Foundation Trust UK
REVIEW RETURNED	29-Apr-2018

GENERAL COMMENTS	This is a well conducted, clearly described longitudinal study cohort study, which acknowledges its limitations.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Alessandra Samelli

Institution and Country: University of Sao Paulo

Please leave your comments for the authors below

The manuscript is well written and the subject matter is current and important. The sample used is huge and this is a great potential of the study. The methodology is well described. The results and discussion are well described. However, there is a serious problem in the study. There is no mention of noise exposure and this aspect, when it comes to workers, can not be considered. Exposure to noise in adults can have important consequences for hearing. Exposure to noise associated with other risk factors such as metabolic diseases, smoking, alcohol consumption, among others, may potentiate hearing loss, since all these agents cause oxidative stress, which has negative consequences for hearing (see Falasca et al. al, 2017 - Noise Induced Hearing Loss: The Role of Oxidative Stress). Therefore, this question must be considered and, if there is no possibility of including the analysis that considers exposure to noise, at least a much more detailed discussion on these aspects should be made.

Thank you for your comment.

As you mentioned, noise exposure is an important risk factor for hearing impairment. Since information on noise exposure was not available in the present study, the confounding due to noise exposure might have biased the association between HbA1c and hearing impairment. Instead of noise exposure, we used job type (professional job, management, office job, sales, service, telegraph, manufacturing, transportation and other) which may be associated with noise exposure level. We confirmed that additional adjustment for job type did not affect the results (Appendix 1 of the previous manuscript).

Furthermore, we performed sensitivity analyses among non-smoking office worker who were less likely to be exposed to occupational noise. We didn't stratify by sex and combined the categories of high HbA1c, due to small number of participants in high HbA1c categories (the figure below).

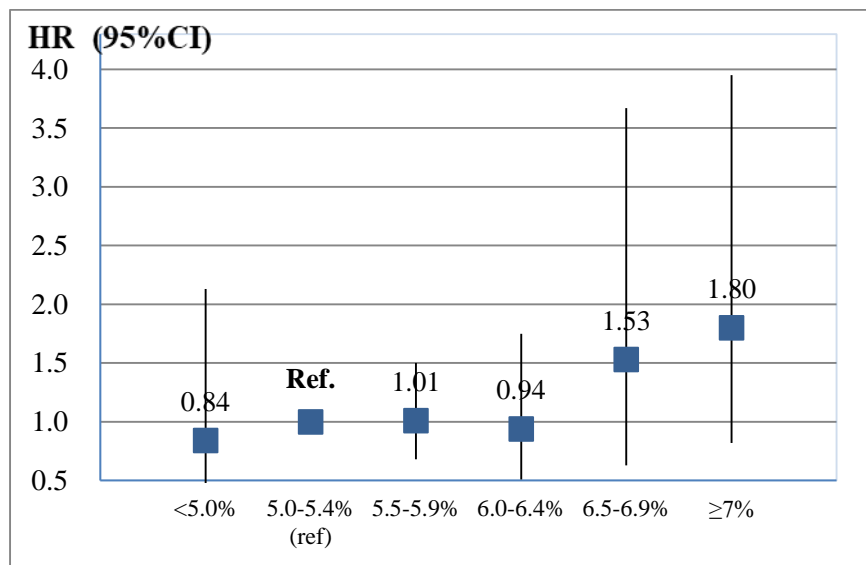


Fig. The association between HbA1c and hearing impairment of high frequency among non-smoking office worker.

We observed the similar tendency between HbA1c and hearing impairment, though the analyses about the association between HbA1c and hearing impairment was underpowered due to the small number of cases. We did not include this figure in the manuscript.

We need more discussion on noise exposure. So, we revised it as follows.

Line283-288:

Before revise:

First, information on noise exposure was not available and thus noise information was not considered in the analyses. However, a previous study reported that the relationship between diabetes and hearing impairment was independent of this variable (37). Moreover, in the present study, HbA1c level was associated with hearing impairment even after accounting for job type in a sensitivity analysis.

After revise:

First, though noise exposure is an important risk factor on hearing impairment (41, 42), information on noise exposure was not available and thus noise information was not considered in the analyses. The present study thus might include the cofounding influence of noise exposure. However, a previous study reported that the relationship between diabetes and hearing impairment was independent of this variable (37). Moreover, in the present study, HbA1c level was associated with hearing impairment even after accounting for job type in a sensitivity analysis.

Line61:

Before revise:

Information on ototoxic drug use, ear surgery, and ear infection was not obtained.

After revise:

Information on noise exposure, ototoxic drug use, ear surgery, and ear infection was not obtained.

Reviewer: 2

Reviewer Name: Joseph Wasson

Institution and Country: East Kent Hospitals University Foundation Trust UK

Please leave your comments for the authors below

This is a well conducted, clearly described longitudinal study cohort study, which acknowledges its limitations.

I appreciate your comment. I will continue to concentrate on improving my study.

VERSION 2 – REVIEW

REVIEWER	Alessandra Samelli University of Sao Paulo - Brazil
REVIEW RETURNED	25-Jun-2018
GENERAL COMMENTS	The suggestions were accepted by the authors. Congratulations on the manuscript.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Alessandra Samelli

Please leave your comments for the authors below

**The suggestions were accepted by the authors. Congratulations on the manuscript.
Thank you for putting it that way.**