

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Acute effects of air pollution on ischaemic stroke onset and deaths: A time-series study in Changzhou, China
AUTHORS	Dong, Huibin; Yu, Yongquan; Yao, Shen; Lu, Yan; Chen, Zhiyong; Li, Guiying; Yao, Yao; Yao, Xingjuan; Wang, Shoulin; Zhang, Zhan

VERSION 1 – REVIEW

REVIEWER	Qun Xu Department of Epidemiology and Biostatistics, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, School of Basic Medicine Peking, Union Medical College, Beijing , China
REVIEW RETURNED	10-Jan-2018

GENERAL COMMENTS	<p>Firstly, the main limitation of this article with exposures measurement was at the community level, likely leading to exposure measurement error.</p> <p>Secondly, the individual address information should be matched with the nearest monitoring data, and use the nearest monitoring data as individual exposures.</p> <p>Thirdly, the author should evaluate whether the monitoring station you used represents a good indicator of individual exposures.</p> <p>Futhermore, a recent study performed in Spain assessed the possible modifying effect of green space and noise in the association between exposure to air pollution and stroke. (PMID: 29310044) The author can refer to this article to extend the modifying effect section.</p>
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REVIEWER	Luiz Alberto Amador Pereira Faculdade de Medicina - Universidade de São Paulo
REVIEW RETURNED	26-Feb-2018

GENERAL COMMENTS	<p>The manuscript is relevant and investigates the possible association between air pollution daily concentrations and stroke (daily hospital admissions and mortality).</p> <p>This is a time-series study well designed for the purpose (acute effects), using an adequate statistical analysis (multiple regression models), quantifying the effects and the lag periods. The discussion is correct. In summary, a good work.</p> <p>I have a few questions that will help the reader:</p> <p>The authors do not justify the affirmation between the lines 14 -24 (page 7) that "The daily mean levels for air pollutants were averaged from all the stations and approximately all the cases recorded in this study resided less than 40 km from the nearest monitoring station. Thus, the monitoring data could be used as an appropriate proxy for personal exposure." I suppose that is an ecological study, using an ecological exposure measure. Based on what information do the</p>
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	<p>authors support such an assertion? What are the limitations of the study? Why the authors selected the ischemic stroke. Hemorrhagic strokes do not have any association with air pollution? Page 13-14 (line 54) "Furthermore, the associations were more pronounced among females, suggesting that females are more susceptible to IS related deaths whe</p>
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VERSION 1 – AUTHOR RESPONSE

To Reviewer #1

Q1: The main limitation of this article with exposures measurement was at the community level, likely leading to exposure measurement error.

Response: We appreciate the reviewer’s suggestion, the exposures measurement was at the community level, which may result in exposure measurement error. However, the real individual exposure was not available to us. Thus, the daily mean levels for air pollutants were averaged from all the stations and approximately all the cases recorded in this study resided less than 40 km from the nearest monitoring station.

Q2: The individual address information should be matched with the nearest monitoring data, and use the nearest monitoring data as individual exposures.

Response: We appreciate the reviewer’s suggestion, but a professional geographical method, inverse distance weighting (IDW) is required when using the nearest monitoring data to scientifically quantify the individual exposure [1]. However, most related and well-designed studies have used the average data from all monitoring stations as individual exposures [2, 3], indicating an appropriate exposure assessment in this study. In addition, the IDW method is not available for us right now due to the technologies limitation.

Q3: The author should evaluate whether the monitoring station you used represents a good indicator of individual exposures.

Response: All the cases included in this study resided less than 40 km from the nearest monitoring station. And it has been suggested that the monitoring data could be used as a proxy for individual exposure among individuals residing less than 40 km from the monitoring station [4-6].

Q4: A recent study performed in Spain assessed the possible modifying effect of green space and noise in the association between exposure to air pollution and stroke. (PMID: 29310044) The author can refer to this article to extend the modifying effect section.

Response: We appreciate the reviewer’s suggestion, and desire to extend the modifying effect section. but in the present study, due to the limitation of database, sex, age and season were the all potential modifications available for us to evaluate.

To Reviewer #2

Q1: The authors do not justify the affirmation between the lines 14 -24 (page 7) that "The daily mean levels for air pollutants were averaged from all the stations and approximately all the cases recorded in this study resided less than 40 km from the nearest monitoring station. Thus, the monitoring data could be used as an appropriate proxy for personal exposure." I suppose that is an ecological study, using an ecological exposure measure. Based on what information do the authors support such an assertion?

Response: We appreciate the reviewer’s suggestion, it has been suggested by the previous work that the monitoring data could be used as a proxy for individual exposure among individuals residing less than 40 km from the monitoring station. And the references have been added.

Q2: What are the limitations of the study?

Response: The limitations were listed on the Article Summary part (page 4).

Q3: Why the authors selected the ischemic stroke. Hemorrhagic strokes do not have any association with air pollution?

Response: We have already assessed the association between air pollution and risk of hemorrhagic strokes, but no statistical result was obtained.

Q4: Page 13-14 (line 54) "Furthermore, the associations were more pronounced among females, suggesting that females are more susceptible to IS related deaths when exposed to gaseous pollutants ". Based on what information do the authors state this?

Response: As described in Table 2, the percentage increases in daily IS related deaths with an IQR increase in NO₂ and SO₂ were 0.37 and 0.434 in females, respectively. They were 0.132 and 0.215, respectively in males. Thus, females are more susceptible to IS related deaths when exposed to gaseous pollutants.

REFERENCES

- 1 Jung CR, Chen WT, Lin Yhsishihashi T, et al. Ambient Air Pollutant Exposures and Hospitalization for Kawasaki Disease in Taiwan: A Case-Crossover Study (2000-2010). *Environ Health Perspect* 2017;125:670-6.
- 2 Nhung NTT, Schindler C, Dien TM, et al. Acute effects of ambient air pollution on lower respiratory infections in Hanoi children: An eight-year time series study. *Environment international* 2018;110:139-48.
- 3 Yin P, Chen R, Wang L, et al. Ambient Ozone Pollution and Daily Mortality: A Nationwide Study in 272 Chinese Cities. *Environ Health Perspect* 2017;125:117006.
- 4 Dockery DW, Luttmann-Gibson H, Rich DQ, et al. Association of air pollution with increased incidence of ventricular tachyarrhythmias recorded by implanted cardioverter defibrillators. *Environ Health Perspect* 2005;113:670-4.
- 5 Wellenius GA, Burger MR, Coull BA, et al. Ambient air pollution and the risk of acute ischemic stroke. *Archives of internal medicine* 2012;172:229-34.
- 6 Xie W, Li G, Zhao D, et al. Relationship between fine particulate air pollution and ischaemic heart disease morbidity and mortality. *Heart (British Cardiac Society)* 2015;101:257-63.

VERSION 2 – REVIEW

REVIEWER	Luiz Alberto Amador Pereira Universidade Católica de Santos - Public Health Post-graduation program, Brasil
REVIEW RETURNED	26-Mar-2018
GENERAL COMMENTS	I accept the author's answers.