

INPLASY PROTOCOL

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Hemorrhagic Stroke for Increase of Ambient Fine Particulate Matter of Diameter $\leq 2.5 \mu\text{m}$: A Systemic Review and Meta-analysis for Cohort Studies

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Review question / Objective: **P:** adults without medical histories of stroke or ischemic heart disease. **I:** exposure to ambient fine particulate matter of 2.5 microns or less in diameter in constant grown levels. **C:** exposure to ambient fine particulate matter of 2.5 microns or less in diameter in a very low level. **O:** occurrence or death of hemorrhagic stroke. **S:** cohort studies.

Condition being studied: Ambient air pollution is a major and significant environmental risk to health in both cities and rural areas. According to the data from World Health Organization, 58% of outdoor air pollution-related premature deaths, especially, the fatal role was due to exposure to fine particulate matter of 2.5 microns or less in diameter (PM_{2.5}), were due to ischaemic heart disease and strokes, thereinto, one third of strokes are hemorrhagic stroke(HS).Therefore, circumstance contaminated by PM_{2.5} is closely related to incidence of HS. Recently, some authors have completed a meta-analysis for cohort studies and concluded that the long-term exposure to PM_{2.5} is an important risk factor for stroke. Yet the nexus between incidence of HS to exposure to ambient PM_{2.5} which increases constantly have not be expounded accurately.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 May 2020 and was last updated on 06 May 2020 (registration number INPLASY202050022).

INTRODUCTION

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microns or less in diameter in constant grown levels. **C:** exposure to ambient fine particulate matter of 2.5 microns or less in diameter in a very low level. **O:** occurrence or death of hemorrhagic stroke. **S:** cohort studies.

Rationale: A hazard ratio(HR) which contains time change and risk ratio is the ratio of two hazard rates which is the percentage of the total number of events per unit time. Authors intend to search for cohorts studies with proportion hazards models and extract the different HRs. Through the synthesis of HRs, a evidence-based conclusion will be acquired according to the pooled HR.

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METHODS

Search strategy: The full strategy of searching literature in PubMed and Cochran is: (((((((((Stroke[MeSH Terms]) OR Strokes[Title/Abstract]) OR "Cerebrovascular Accident*" [Title/Abstract]) OR CVA*[Title/Abstract]) OR Apoplexy[Title/Abstract]) OR "Vascular Accident*, Brain"[Title/Abstract]) OR "Brain Vascular Accident*" [Title/Abstract]) OR stroke[Title/Abstract])) AND (((((((("Air Pollution"[MeSH Terms]) OR "Pollution, Air"[Title/Abstract]) OR "Air Quality"[Title/Abstract]) OR "Particulate Matter"[MeSH Terms]) OR "Airborne Particulate Matter"[Title/Abstract]) OR "Particulate Matter, Airborne"[Title/Abstract]) OR "Air Pollutant*, Particulate"[Title/Abstract]) OR "Particulate Air Pollutant*" [Title/Abstract])

OR "Pollutant*, Particulate Air"[Title/Abstract]) OR "Ambient Particulate Matter"[Title/Abstract]) OR "Particulate Matter, Ambient"[Title/Abstract]). The full strategy of searching literature in Embase is: (exp Stroke or Stroke\$:ab,ti or 'Cerebrovascular Accident\$':ab,ti or CVA\$:ab,ti or Apoplexy:ab,ti or 'Vascular Accident\$, Brain':ab,ti or 'Brain Vascular Accident\$':ab,ti or stroke:ab,ti) and (exp 'Air Pollution' or 'Pollution, Air':ab,ti or 'Air Quality':ab,ti or exp 'Particulate Matter' or 'Airborne Particulate Matter':ab,ti or 'Particulate Matter, Airborne':ab,ti or 'Air Pollutant\$, Particulate':ab,ti or 'Particulate Air Pollutant\$':ab,ti or 'Pollutant\$, Particulate Air':ab,ti or 'Ambient Particulate Matter':ab,ti or 'Particulate Matter, Ambient':ab,ti).

Participant or population: Adults without medical histories of stroke or ischemic heart disease.

Intervention: Exposure to ambient fine particulate matter of 2.5 microns or less in diameter in constant grown levels.

Comparator: Exposure to ambient fine particulate matter of 2.5 microns or less in diameter in a very low level.

Study designs to be included: Cohort studies.

Eligibility criteria: A cohort studies will be included which performed a survival analysis through proportional hazards model of occurrence or death of hemorrhagic stroke which was due to exposure to ambient fine particulate matter of 2.5 microns or less in diameter with different grown level.

Information sources: All of studies were independently searched by two authors separately from three open electronic databases : PubMed, Cochran, Embase.

Main outcome(s): Participates will not be included to endpoint of observation until occurrence or death of hemorrhagic stroke which was due to exposure to ambient fine particulate matter of 2.5 microns or less in

diameter with different grown level happens. The diagnosis of hemorrhagic stroke will be defined by International Classification of Diseases.

Additional outcome(s): N/A.

Data management: All the data in included studies, values and credibility interval of hazard ratios from each proportional hazards model adjusted by different factors, were independently extracted by two authors separately.

Quality assessment / Risk of bias analysis: All the studies were independently assessed by two authors separately referring to Newcastle - Ottawa Quality Assessment Scale Cohort Studies which contained assessment of selection of participates included, comparability and outcome observed in a cohort study.

Strategy of data synthesis: The values and credibility intervals of hazard ratios from proportional hazards model adjusted by the least and the most factors in each study included will be synthesized by Random Effects Model module in Software for Statistic and Data Science to conclude pooled hazard ratios. If the heterogeneity has statistical significant(I-square surpasses 50% too much and P value is lower than 0.05), subgroups analysis should be used to perform. The data synthesis will be independently completed by two authors separately.

Subgroup analysis: If the heterogeneity of synthesis of values and credibility intervals of hazard ratios from proportional hazards model adjusted by the least and the most factors in each study included has statistical significance, try to check the difference in grown levels of ambient fine particulate matter of 2.5 microns or less in diameter and different factors adjusted. Then data in each subgroups separated by grown levels or relative factors should be synthesized independently. The subgroup analysis will be independently completed by two authors separately.

Sensibility analysis: The sensibility analysis will be completed by comparing data synthesis and subgroup analysis performed by Random Effects Model module in Software for Statistic and Data Science to those performed by Fixed Effects Model module in the software. If the difference in heterogeneity and synthesis have nothing in statistical significance, the outcome in analysis will be stable. Or the strategy of data analysis should be modified. The sensibility analysis will be independently completed by two authors separately.

Language: Language limits will not be imposed on the search.

Country(ies) involved: China, Canada, Netherlands, Korea, United Kingdom.

Other relevant information: N/A.

Keywords: Ambient Pollution; PM2.5; Hemorrhagic Stroke; Meta-analysis.

Dissemination plans: The meta-analysis and systemic review completed will be published in a journal added to Science Citation Index with a high influence factors such as Stroke, World Neurosurgery.

Contributions of each author:

Author 1 - Zhao Kai - Author 1 drafted the manuscript.

Author 2 - Du Chaonan - The author provided statistical expertise.

Author 3 - Guo Yu - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.

Author 4 - Yang Mingfei - The author read, provided feedback and approved the final manuscript.