INTRODUCTION

Review question / Objective: The purpose of this study was to examine the differences in the incidence of rheumatoid arthritis between those exposed to passive smoking and those not exposed to passive smoking.

Condition being studied: The investigators have gained some understanding of this topic through preliminary searches. The investigators of this study all have a foundation of study related to the discipline of rheumatology and immunology, and all have background knowledge of literature search and statistics required for Meta-analysis. Patients with rheumatoid arthritis in the case-control study and all members included in the study in the cohort study.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 May 2022 and was last updated on 08 May 2022 (registration number INPLASY202250046).

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Review Stage at time of this submission: The review has not yet started.

Conflicts of interest: None declared.
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METHODS

Participant or population: Patients with rheumatoid arthritis in the case-control study and all members included in the study in the cohort study.

Intervention: Passive smoking.

Comparator: Not exposed to passive smoking.

Study designs to be included: Case-control studies or cohort studies.

Eligibility criteria: We included relevant case-control studies and cohort studies of passive smoking and risk of rheumatoid arthritis.

Information sources: We searched 4 electronic databases, including Pubmed, The Cochrane Central Register of Controlled Trials, Web of Science and EMBASE.

Main outcome(s): Differences in the incidence of rheumatoid arthritis in passive smoking exposed and non-exposed populations.

Quality assessment / Risk of bias analysis: Quality of each included study quality was assessed by 2 reviewers by using the Newcastle Ottawa Quality Assessment Scale (NOQAS) for cohort and case-control studies, with each study judged on the basis of study group selection, comparability between groups, exposure, and determination of outcome. Scores ranged from 0 (poor) to 9 (excellent). The current work was conducted in accordance with the recommendations of the PRISMA Statement. When the number of studies was sufficient ($N \geq 10$), publication bias was assessed using an inverted funnel plot.

Strategy of data synthesis: As for the selection of statistical model, we first used the $\chi^2$ test and $I^2$ values to assess the heterogeneity between studies: if $P > 0.1$ and $I^2 < 50\%$ indicated good homogeneity between studies, a fixed-effects model was used for statistical analysis; conversely, a random-effects model was selected under the premise of excluding clinical heterogeneity; and sensitivity analysis or subgroup analysis was performed for factors that might lead to heterogeneity. We used Stata 16.0 (StatCorp LLC, Texas, The United States of America) to present the effect sizes and integrated RRs and their 95% CIs for each study using forest charts.

Subgroup analysis: In the subgroup analysis, to assess the effect of passive smoking on the incidence of RA, we will analyze both from the following two aspects: (1) grouping according to the study type: case-control study or cohort study; (2) grouping according to the population exposed to passive smoking—lived with smokers since age 18, childhood parental smoking and maternal smoking during pregnancy (in utero exposure).

Sensitivity analysis: A sensitivity analysis was carried out to investigate the influence of individual studies and the stability of the results by omitting one study at a time. Publication bias was assessed using Begg's regression asymmetry test. $P<0.05$ was considered representative of statistically significant publication bias.

Country(ies) involved: China.

Keywords: Passive smoking, Rheumatoid arthritis, Incidence, Meta-analysis.

Contributions of each author:
Author 1 - Xieyu Zhang was involved in the design of the study, writing of the manuscript and data collection. Under the supervision of Wei Cao, Xinwen Zhang analyzed the data.
Author 3 - Yue Yang was involved in the design of the study, writing of the manuscript and data collection.
Author 4 - Jiahe Zhao was involved in data collection and collation. Wei Cao was involved in the design of the study and supervised the statistical analysis of the study data and assisted in writing the manuscript.
Author 5 - Kai Zhi was involved in data collection and collation. Jiahe Zhao was involved in data collection and collation.
Author 6 - Wei Cao was involved in the design of the study and supervised the statistical analysis of the study data and assisted in writing the manuscript. Zhi KAI was involved in data collection and collation.