INPLASY PROTOCOL

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Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

Conflicts of interest:
None declared.

Hyperuricemia increases the risk of atrial fibrillation: a systematic review and meta-analysis

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Review question / Objective: Association between HUA and AF remains unclear, for which the present meta-analysis will systematically review clinical evidence and may give suggestions for therapy of those AF patients with gout or HUA.

Condition being studied: Hyperuricacidemia (HUA) is a metabolic disease caused by purine metabolism and imbalance of uric acid production and excretion, with a uric acid level > 7.0 mg/dL in men and > 5.7 mg/dL in women. Atrial fibrillation is known as a common cardiac disease.

Information sources: PubMed, Clinical trial, Embase database, Cochrane Library, China national knowledge infrastructure (CNKI), Epigraph DB (https://epigraphdb.org/), DigiZeitschriften (http://www.digizeitschriften.de/) and Web of Science. We will ask authors for literatures if possible.

INTRODUCTION

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excretion, with a uric acid level > 7.0 mg/dL in men and > 5.7 mg/dL in women. Atrial fibrillation is known as a common cardiac disease.

METHODS

Participant or population: General population.

Intervention: We will include observational studies, including retrospective cohort studies, cross-sectional studies, and prospective cohort studies. The exposure we will study was mainly hyperuricemia (HUA).

Comparator: We will include observational studies, including retrospective cohort studies, cross-sectional studies, and prospective cohort studies. The comparators will be those individuals without hyperuricemia and with or not atrial fibrillation.

Study designs to be included: We will include representative cohort studies, cross-sectional studies and prospective cohort studies.

Eligibility criteria: We will exclude studies that may lead to an incredible conclusion. We will include cross-sectional, retrospective and prospective cohort studies. Randomized controlled trials will be excluded. The reason is that randomized controlled trials are too rare to lead to independently certain results, as introduced later. And difference in study designing will bring uncertainty to the evidence provided in this study. Study type should be clearly defined. Cross-sectional studies should clearly introduce the sources of epidemiological data. Sources as public health databases, hospital medical records, or insurance agencies will be acceptable . The number of participants should be sufficient to avoid contingency. Any study of participants less than 200 will be excluded. Studies will be excluded if with too many complications unrelated to AF enrolled. We will include only studies that all the follow-up work completed to ensure the whole data is available. Criteria

of hyperluricacid or AF should be defined clearly, which should be consistent with the universal knowledge. Studies get "Critical risk" in overall will be excluded. Retrospective studies reporting association between AF and HUA will be included. Participants should be defined with hyperuricemia directly. Case reports, protocols or trials with incomplete follow-up will be excluded.

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Main outcome(s): To evaluate the proportion of atrial fibrillation in people with and without hyperuricemia.

Quality assessment / Risk of bias analysis: Quality evaluation will be operated by R version 4.1.2, using the revised Cochrane risk-of-bias tool for randomized trials (ROB2). One reviewer (G.Z.) will evaluate all studies included in seven domains: 1. Bias due to confounding 2. Bias due to selection of participants 3. Bias in classification of interventions 4. Bias due to deviations from intended interventions 5. Bias due to missing data 6. Bias in measurement of outcomes 7. Bias in selection of the reported result. Risk of each study will be labelled as "Low risk", "Moderate risk", "Serious risk" and "Critical risk".

Strategy of data synthesis: Data synthesis will be operated on R version 4.1.2, using the package "meta" (R Project for Statistical Computing) (R Core Team. R: a language and environment for statistical computing. Vienna R Foundation for Statistical Computing; 2019. https://www.R-project.org). Risk ratio (RR) and its 95 % confidence interval will be used to evaluate the proportion of atrial fibrillation in people with and without hyperuricemia. Studies will be sub-grouped and regressed to detect possible sources of heterogeneity and potential influencing factors of AF

proportion. All statistical effects will be calculated in a random effect model, with a two-tailed $\alpha=0.05$ set as the statistical significance. The Cochrane's Q test and I^2 will be calculated as measures of heterogeneity. I^2 values of 25%, 50%, 75% will be thought to indicate a low, moderate or high heterogeneity.

Subgroup analysis: Important covariates such as race, country or study design will be used as a classification basis for subgroup analysis. Subgroup analysis is intended to test heterogeneity and factors that may affect results.

Sensitivity analysis: Sensitivity analysis will be performed using the function "metainf", package "meta" on R version 4.1.2.

Country(ies) involved: China.

Keywords: hyperuricacidemia; atrial fibrillation; prevalence.

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