INPLASY PROTOCOL

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

Conflicts of interest: **NO.**

Association between microRNA 25 expression in serum and lung cancer: a protocol of systematic review and meta-analysis

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Review question / Objective: **Is microRNA 25 (mRNA 25) expression in serum associated with patients with lung cancer (LC)?**
Condition being studied: **MicroRNA 25 and lung cancer.**
Information sources: **We will retrieve Cochrane Library, PubMed, EMBASE, Web of Science, Allied and Complementary Medicine Database, VIP database, and China National Knowledge Infrastructure from inceptions to the present. All electronic database sources will be searched from inception to the present without limitations of language and publication status. The search strategy for Cochrane Library is created. We will also adapt similar search strategies and will apply them to the other electronic databases. We will include all eligible case-controlled studies that report associations between mRNA 25 expression in serum and LC. In addition, we will also examine other literature sources, including conference proceedings and reference lists of related reviews.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 April 2020 and was last updated on 10 April 2020 (registration number INPLASY202040056).

INTRODUCTION

Review question / Objective: **Is microRNA 25 (mRNA 25) expression in serum associated with patients with lung cancer (LC)?**

Condition being studied: **MicroRNA 25 and lung cancer.**

METHODS

Participant or population: **This study will include patients with histopathology-proven LC and normal participants without restrictions of race, age, gender, and educational background.**

Intervention: **Experimental group: mRNA 25 expression in serum was detected in all patients with histopathology-proven LC.**

Comparator: **Control group: mRNA 25 expression in serum was detected in the normal participants.**

Study designs to be included: All case-controlled studies on exploring the associations between mRNA 25 expression in serum and LC will be included.

Eligibility criteria: All case-controlled studies compared the association between mRNA 25 expression in serum of LC patients or normal participants.

Information sources: We will retrieve Cochrane Library, PubMed, EMBASE, Web of Science, Allied and Complementary Medicine Database, VIP database, and China National Knowledge Infrastructure from inceptions to the present. All electronic database sources will be searched from inception to the present without limitations of language and publication status. The search strategy for Cochrane Library is created. We will also adapt similar search strategies and will apply them to the other electronic databases. We will include all eligible case-controlled studies that report associations between mRNA 25 expression in serum and LC. In addition, we will also examine other literature sources, including conference proceedings and reference lists of related reviews.

Main outcome(s): The primary outcome is levels of mRNA-25 expression in serum (as measured by real-time polymerase chain reaction test).

Additional outcome(s): The secondary outcomes are relevant LC parameters, including pathological types, tumor-node-metastasis stages, lymph node metastasis, and tumor markers.

Data management: Two contributors will independently extract data according to the predefined and standardized data extraction sheet. Any conflicts between two contributors will be resolved by another contributor through consultation. The following data will be extracted from each trial: first author, journal, time of publication, region, race, age, sex, diagnostic criteria, inclusion and exclusion criteria, sample size, study design, types of targeted subjects, outcome indicators, conflict of interest. If we identify any missing or insufficient information, we will contact original authors to obtain that.

Quality assessment / Risk of bias analysis: Study quality of each included study will be evaluated using Newcastle-Ottawa Scale. Two independent contributors will assess study quality, respectively. Any difficulties encountered between two contributors will be solved with another contributor.

Strategy of data synthesis: This study will utilize RevMan V.5.3 software for data synthesis and data analysis. We will estimate the treatment effect of continuous data as mean difference or standardized mean difference and 95% confidence intervals (CIs), and dichotomous data using risk ratio and 95% CIs. We will identify heterogeneity across eligible trials using I^2 statistic. It is defined as follows: $I^2 \leq 50\%$ indicates homogeneity and a fixed-effect model will be employed, and $I^2 > 50\%$ means significant heterogeneity and a random-effect model will be utilized. We will carry out a meta-analysis if sufficient data are collected from eligible studies with homogeneity. On the other hand, we will perform a subgroup analysis to examine the sources of heterogeneity. In addition, we will also conduct a narrative summary. We will report this study results as a narrative summary by providing detailed written commentary to present study findings, study quality, and outcome indicators (e.g. mRNA-25 expression).

Subgroup analysis: We will carry out subgroup analysis to check sources for significant heterogeneity based on the different types of study characteristics, study methods, and outcome indicators.

Sensibility analysis: We will perform sensitivity analysis to explore the robustness and stability of study findings by removing low quality studies.

Country(ies) involved: China.

Keywords: Lung cancer; microRNA 25; association; case-controlled study.