INTRODUCTION

Review question / Objective: Recently, lung cancer has become the most common cause of cancer-related death, several studies indicate that the cytochrome P450 2A13 (CYP2A13) polymorphisms may be correlated with lung cancer susceptibility, but the results have been inconsistent and inconclusive. Therefore, the aim of this meta-analysis is to provide a precise conclusion on the potential association between CYP2A13 polymorphisms and the risk of lung cancer based on case-control studies.
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**Condition being studied:** The PubMed, Embase, Cochrane Library, Web of Science and China National Knowledge Infrastructure (CNKI) databases will be searched for case-control studies published up to September 2020. Odds ratio (OR) and 95% confidence interval (95% CI) were used to determine the effects of the CYP2A13 polymorphism on lung cancer risk, respectively.

**METHODS**

**Participant or population:** Lung cancer population.

**Intervention:** using case-control study method to assess the relationship of CYP2A13 polymorphisms with lung cancer risk.

**Comparator:** non-lung cancer or health population.

**Study designs to be included:** case-control study.

**Eligibility criteria:** (1) using case-control study method to assess the relationship of CYP2A13 polymorphisms with lung cancer risk. (2) the size of the sample, odds ratios (ORs), and their 95% confidence intervals (CIs) were provided. (3) in the case of multiple publications from the same study group, the most complete and recent results will be used.

**Information sources:** We will search the PubMed, Cochrane Library, Web of Science, CNKI databases, and the time period for the reference searches was from the first available article to September 2020.

**Main outcome(s):** This meta-analysis will summarize the association between CYP2A13 polymorphisms and the risk of lung cancer. The results of this meta-analysis will be submitted to a peer-reviewed journal for publication.

**Quality assessment / Risk of bias analysis:** The quality of the included studies will be independently assessed by the Newcastle-Ottawa Quality Assessment Scale (NOS) [27]. The evaluation project consisted of 8 parts, and except for the fifth evaluation criterion of 2 points, the scores of the other items are all 1 point. The total scores of the NOS range from 0 points to 9 points. If the total score of the 8 items is greater than or equal to 7 points, the quality of studies is considered reliable.

**Strategy of data synthesis:** The statistical analysis will be performed by using Review Manager 5.3. Pooled odds ratios and 95% confidence intervals will be applied to estimate the strength of associations between the CBS gene polymorphisms and lung cancer risk. The heterogeneity between the included studies will be judged on the basis of P and I² values. Values of P>0.10 and I²<50% indicate that the fixed effect model could be used in this meta-analysis. However, values of P50% indicate the existence of significant heterogeneity. We will identify the source of heterogeneity and perform further analysis, and the random effects model will be used after excluding the effects of significant clinical heterogeneity.

**Subgroup analysis:** To further study the effect of sample size, diagnosis methods and ethnicity on heterogeneity, subgroup analysis will be performed.

**Sensibility analysis:** We will perform a sensitivity analysis to verify the robustness of the study results. This will be achieved by assessing the impact of the sample size, high risk of bias, missing data, and selected models. Following the analyses, if the quality of a study is judged to be low, it will be removed to ensure the robustness of the results.

**Country(ies) involved:** China.

**Keywords:** Cytochrome P450 2A13, Polymorphism, Lung Cancer, Meta-analysis.
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