INPLASY PROTOCOL

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Review Stage at time of this submission: **Data extraction.**

Conflicts of interest:
The authors declare that they have no competing interests.

A comprehensive evaluation of single nucleotide polymorphisms associated with gastric cancer risk: a protocol for systematic review and network meta analysis

Ye, Z[1]; Hu, Q[2]; Zheng, J[3]; Zhang, C[4];Zhu, X[5]; Tang, Y[6].

Review question / Objective: **Do PSCA rs2976392,XPG rs751402,VEGF rs3025039 gene polymorphisms have any associations with a higher gastric cancer risk?**
Condition being studied: **Gastric cancer,SNPs,gene polymorphisms.**
Information sources: **Studies published through January 2020 which be included in our meta-analysis were identified from PubMed, Web of Science, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), the Chinese Science and Technology Periodical Database (VIP) and Wanfang databases. There are no restrictions on literature language. The following search terms will be used for the search: "single nucleotide polymorphism", "SNP", "gastric cancer", "stomach cancer".**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 April 2020 and was last updated on 22 April 2020 (registration number INPLASY202040132).

INTRODUCTION

Review question / Objective: **Do PSCA rs2976392,XPG rs751402,VEGF rs3025039 gene polymorphisms have any associations with a higher gastric cancer risk?**

Condition being studied: **Gastric cancer,SNPs,gene polymorphisms.**

METHODS

Participant or population: **Participants affected by GC and was taken serumsamples before prior chemoradiotherapy will be included.**

Intervention: Associated with gastric cancer gene polymorphisms.

Comparator: Noncancer controls may be healthy or have non-malignant diseases.No restrictions were placed on age, gender, country, or tumor stage.

Study designs to be included: Case-control study, published in either English or Chinese that concern the susceptibility of the SNPs to the GC, will be integrated into this review.

Eligibility criteria: This study will include RCTs and case-control study that comparing the risk of different gene polymorphisms for patients with GC.

Information sources: Studies published through January 2020 which be included in our meta-analysis were identified from PubMed, Web of Science, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), the Chinese Science and Technology Periodical Database (VIP) and Wanfang databases. There are no restrictions on literature language. The following search terms will be used for the search: "single nucleotide polymorphism", "SNP", "gastric cancer", "stomach cancer".

Main outcome(s): Gastric cancer risk comparisons.

Quality assessment / Risk of bias analysis: The methodological quality of data was assessed based on the STREGA statement(8). Two reviewers conducted the rating independently and a third reviewer was consulted for consensus if disagreement occurred.

Strategy of data synthesis: For each meta-analysis, odds ratio (OR) with 95% confidence intervals (CIs) will be calculated in fixed OR random effects.The fixed-effect model would be employed if I2 < 50%,which suggested low heterogeneity among include studies.Otherwise,random-effect model will be used.If we have enough great meaningful SNPs's data,subgroup analysis would be used to analysis the source of the heterogeneity. STATA software/MP 14.0 was applied to analyze the relationship between single nucleotide polymorphisms and gastric cancer. The random-effects model was used. The model parameters were estimated using the Markov chain Monte Carlo method of Gibbs sampling. The results are reported as the odds ratio (OR) with 95% confidence intervals (CIs). To evaluate the inconsistency between direct and indirect effect estimates for the same comparisons, we evaluated each closed loop in the network. In a closed loop, we employed the inconsistency factor (IF) to evaluate heterogeneity among the included studies. To rank the SNPs and their gene models, we used the surface under the cumulative ranking probabilities (SUCRA).We further compared genetic models to select the most appropriate model using the algorithm by Thakkinstian et al. To assess the authenticity of the normally significant SNPs under the most appropriate genetic model determined by network meta-analysis or Thakkinstian' algorithm, false positive report probability (FPRP) was calculated assuming three levels of prior probabilities (low: 0.1; moderate: 0.01; high: 0.001) and an OR of 1.5, as previously described. Significant SNPs with a FPRP value < 0.2 were considered noteworthy. Thakkinstian's algorithm was also used to evaluate the best model to be the SNP obtained from the previous optimal gene model in the reticular meta-analysis.

Subgroup analysis: We will conduct a subgroup analysis of the SNPs most associated with gastric cancer , according to race, type of age, sex, etc.

Sensibility analysis: Sensitivity analysis will be conducted to check the robustness and reliability of pooled outcome results.

Country(ies) involved: China.

Keywords: Gastric cancer; case-control study; model of inheritance; network meta-analysis; susceptibility.