

INPLASY PROTOCOL

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

Conflicts of interest: The
author declared that they
have no conflict of interest.

A comprehensive evaluation of association between homocysteine levels and single nucleotide polymorphisms with hypertension risk : A protocol of systematic review and network meta-analysis

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Review question / Objective: To explore the relationship between homocysteine level and single nucleotide polymorphism and hypertension risk.

Condition being studied: SNPs, homocysteine, hypertension, gen polymorphism.

Information sources: Data will search from the following electronic databases: PubMed, Web of Science, Embase, Cochrane Library ,China National Knowledge Infrastructure (CNKI), the Chinese Science and Technology Periodical Database (VIP) and Wan fang databases, and Chinese Biomedical Literature Database (CBM). With publications up until March 2020 ,to find out this meta-analysis relative studies, The search strategy was based on the following search terms: “single nucleotide polymorphism”, “SNP”, “homocysteine”, and “hypertension”.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 May 2020 and was last updated on 01 May 2020 (registration number INPLASY202050002).

INTRODUCTION

Review question / Objective: To explore the relationship between homocysteine level and single nucleotide polymorphism and hypertension risk.

Condition being studied: SNPs, homocysteine, hypertension, gen polymorphism.

METHODS

Participant or population: Participants affected by HCY and HTN. Studies have detailed allele and genotype frequencies reported. If SNPs demonstrated a departure from Hardy-Weinberg equilibrium (HWE) in controls were excluded. When there were multiple publications from the same population, only the largest study was included.

Intervention: Association between homocysteine levels and single nucleotide polymorphisms with hypertension.

Comparator: Nonhypertension subjects. No restrictions were placed on age, gender, country, or type of hypertension.

Study designs to be included: Case-control study, published in either English or Chinese that concern the association between SNPs and HCY levels with hypertension risk.

Eligibility criteria: This study will include RCTs and case-control study that comparing the different gene polymorphisms for patients, resulting in HCY changes and thus increasing the hypertension risk.

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Main outcome(s): Snp is most correlated with HTN risk.

Quality assessment / Risk of bias analysis: The quality of this meta analysis was

evaluated through a checklist originated from Strengthening the Reporting of Genetic Association (STREGA) recommendations for reports genetic association studies. Two investigators independently rating. If disagreement occur, resolved by discussion or consultation with a third investigator.

Strategy of data synthesis: Statistical analyses were calculated with STATA 14.0, Hardy-Weinberg equilibrium (HWE) was evaluated for each study by Chi-square test in control groups, and $P < 0.05$ was considered a significant departure from HWE. We analyzed six model: allele contrast model, homozygous model, heterozygous model, dominant model, recessive mode and additive model. Calculated fixed- or random- effects pooled odds ratio (OR) with 95% confidence intervals (CIs) for pairwise. The choice of effect model depends on heterogeneity. Heterogeneity was quantified with the I^2 statistic and P value; a I^2 statistic $< 50\%$ and a $P > 0.1$ indicated low heterogeneity between studies, in which case the fixed-effect model (based on Mantel-Haenszel method) was employed; otherwise, the random-effects model (based on DerSimonian-Laird method) was applied. Statistical heterogeneity among the studies was checked by chi-square-based Q -test. In this meta-analysis, genes with significant heterogeneity were analyzed in subgroups. A random-effects network meta-analysis within a Bayesian framework was conducted using the GeMTC software (v 0.14.3). Four parallel Markov chain Monte Carlo simulations were run for a 20,000-stimulation burn-in phase and an additional 50,000-stimulation phase. Convergence was satisfied with a potential scale reduction factor (PSRF) value of 1.0 as the cut-off value. When significant deviations were detected, we use an inconsistency model; otherwise, the consistency model was used. This Bayesian approach was used to rank the probability of each genetic model for risk assessment and corresponding rank probability plots were generated. We further compared genetic models to select the most appropriate

model using the algorithm by Thakkinstian et al. Diagnostic meta-analysis was conducted to determine sensitivity and specificity of SNPs in predicting HTN risk using the Meta-DiSc software.

Subgroup analysis: Subgroup analysis was conducted according to age, race and gender.

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

Country(ies) involved: China.

Keywords: Single nucleotide polymorphism, homocysteine, hypertension, network meta-analysis.

Contributions of each author:

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