**Meta-analysis on Genetic Association Studies Checklist | PLOS ONE**

|  |  |  |
| --- | --- | --- |
|  | Item | Section name and paragraph number within manuscript |
|  | **Introduction** |  |
| 1 | Provide a detailed justification for the polymorphism studied; if a single polymorphism was analyzed, give details as to why others were not included in the meta-analysis. | This manuscript focused on DNA methylation of P16 gene, but not polymorphism. |
| 2 | Provide a detailed justification for the population(s) and clinical condition studied. | Materials and Methods: Search Strategy  Paragraph: 4 |
|  | **Methods** |  |
| 3 | Provide full details of the search strategy employed; outline the full electronic search strategy –specific combination of keywords and any limits applied- for at least one database. Specify whether synonyms of polymorphisms/genes (e.g. SNP number) were searched. | Materials and Methods: Search Strategy  Paragraph: 4 |
| 4 | Report full details on the inclusion and exclusion criteria applied for selecting studies.  *Please list the excluded articles and the reasons for exclusion of each article in a supplementary file.* | Materials and Methods: Study Selection  Paragraph: 5 |
| 5 | Provide details on how the quality of the studies included in the analyses was assessed. | Materials and Methods: Data Extraction and Quality Assessment  Paragraph: 6 |
| 6 | Describe steps taken to contact study authors to identify additional studies and to request missing data. | All full- text of paper idenfitied had been obtained, and there was no missing data. |
| 7 | Describe how environmental effects were adjusted for, if this adjustment was not conducted, outline the reasons for this. | No.  Reason:The original studies did not conduct the adjustment for environmenttal effects. |
| 8 | Describe the methods of handling heterogeneity/between-study variance. | Materials and Methods: Statistical Analysis  Paragraph: 7 |
| 9 | Describe how the Hardy-Weinberg equilibrium and linkage disequilibrium were assessed. | This manuscript focused on DNA methylation of P16 gene, but not polymorphism. |
| 10 | Describe and justify the choice of model for the analyses (per-allele vs per-genotype vs genetic model-free, random effects vs fixed effects). | Materials and Methods: Statistical Analysis  Paragraph: 7 |
| 11 | Describe whether a sensitivity analysis has been completed. | Results: Sensitivity Analysis  Paragraph: 10 |
| 12 | Describe whether an assessment of the effects of population stratification has been conducted. | Results: Meta-regression and Subgroup Analysis  Paragraph: 11-12 |
| 13 | Describe whether study-specific results have been assessed and if so the reasons for this (e.g. forest plot). | Results: Combining Results of Included Studies and Publication bias  Paragraph: 9, 13 |
|  | **Results** |  |
| 14 | Include flow diagram for the studies included in the meta-analysis as the first figure for the manuscript | Results: Study Characteristics  Paragraph: 8 |
| 15 | Report details on allele/genotype prevalence. | This manuscript focused on DNA methylation of P16 gene, but not polymorphism. |
| 16 | Report the effect size estimates and p values for each analysis. | Results: Combining Results of Included Studies  Paragraph: 9 |
|  | **Discussion** |  |
| 17 | Discuss the limitations of the meta-analysis, including genotyping errors/bias and publication bias. | Discussion  Paragraph: 17 |
| 18 | If the meta-analysis identifies an association within a subgroup of the population studied but not another, discuss the implications of these results, and if applicable the possibility of subgroup-specific publication bias. | Discussion  Paragraph: 16 |
| 19 | Discuss the suitability of the sample size employed to the research question and the power of the study. | NA |