

Abstract

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Meta-analysis: apolipoprotein E genotypes and risk for coronary heart disease.

Song Y, Stampfer MJ, Liu S.

Brigham and Women's Hospital, Harvard Medical School, and Harvard School of Public Health, Boston, Massachusetts 02215, USA.

BACKGROUND: Apolipoprotein E (apoE) genotypes play critical roles in lipid metabolism and are believed to influence risk for coronary heart disease (CHD). Despite many population studies, however, the impact of apoE polymorphism on risk for CHD remains uncertain.

PURPOSE: To qualitatively and quantitatively assess the evidence regarding the relation of apoE polymorphism to CHD risk.

DATA SOURCES: All relevant reports and references from original and review papers published from 1966 to January 2004.

STUDY SELECTION: Predefined criteria were used to identify 48 relevant studies.

DATA EXTRACTION: A summary database that contained variables of study design, study sample and ethnicity, sex, apoE genotypes, CHD end points, plasma lipid levels, and other CHD risk factors was developed.

DATA SYNTHESIS: The authors qualitatively evaluated many potential sources of heterogeneity. To quantify the extent of heterogeneity and assess the consistency of apoE-CHD associations, stratified analyses were conducted using the classic random-effects model. To further incorporate uncertainty due to between-study variation, the pooled odds ratios (ORs) and 95% credible intervals (CrIs) were estimated by using a Bayesian hierarchical model. Finally, the robustness of the pooled estimates was tested in multiple sensitivity analyses. Compared with individuals with the epsilon3/3 genotype, carriers of the apoE epsilon4 allele had a 42% higher risk for CHD (OR, 1.42 [95% CrI, 1.26 to 1.61]). The epsilon2 allele had no significant association with CHD risk (OR, 0.98 [CrI, 0.66 to 1.46]).

LIMITATIONS: This meta-analysis did not include unpublished data or studies published in languages other than English.

CONCLUSIONS: Inadequate statistical power, differences in geographic and ethnic background, allele frequency, sex, CHD phenotypes, study design, and potential gene-environment interactions may have contributed to the conflicting results of previous studies. The apoE epsilon4 allele is a significant risk factor for CHD.

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