INPLASY PROTOCOL

To cite: Zhang et al. Association between extremely high-density lipoprotein cholesterol and adverse cardiovascular outcomes: A protocol for systematic review and meta-analysis. Inplasy protocol 202330022. doi: 10.37766/inplasy2023.3.0022

Received: 06 March 2023

Published: 06 March 2023

Corresponding author:
Yongsheng Huang

lingxi1622@163.com

Author Affiliation:
Department of Cardiology, Affiliated Hospital of Changchun University of Chinese Medicine.

Review Stage at time of this submission: **Piloting of the study selection process.**

Conflicts of interest:
None declared.

Association between extremely high-density lipoprotein cholesterol and adverse cardiovascular outcomes: A protocol for systematic review and meta-analysis

Zhang, GW[1]; Guo, JJ[2]; Jin, HG[3]; Wei, XJ[4]; Zhu, X[5]; Jia, WT[6]; Huang, YS[7].

Review question / Objective: **The current research aimed to investigate the association between extremely high HDL-C and adverse cardiovascular outcomes in cohort studies using a systematic review and meta-analysis.**
Eligibility criteria: **Inclusion criteriaCohort studies will be included if the research (a) assess the association between extremely high HDL-C levels and risks of all-cause and cardiovascular death, stroke, MI, and heart failure; (b) containe relative risks (RR), hazard ratios (HR), or odds ratios (OR) of 95% confidence intervals (CI); (c) include estimates of at least three categories of HDL-C measurements in the analysis; (d) consider the normal levels of HDL-C as the reference range. Exclusion criteriaThe following research types including case-control studies, animal experiments, irrelevant outcomes, no extremely high levels of HDL-C, duplicate publications, reviews, meta-analyses, non-English language, abstracts, letters, case reports, and articles for which the full text will be not available were excluded. Besides, repetitive publications with an identical cohort, including HDL-C levels reported the most abundant data, or data with a larger number of outcomes or sample sizes will be excluded.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 March 2023 and was last updated on 06 March 2023 (registration number INPLASY202330022).

INTRODUCTION

Review question / Objective: **The current research aimed to investigate the association between extremely high HDL-C and adverse cardiovascular outcomes in cohort studies using a systematic review and meta-analysis.**

Condition being studied: High-density lipoprotein cholesterol (HDL-C) has been identified as a risk factor for atherosclerotic cardiovascular disease (CVD), and numerous pieces of evidence have indicated the presence of a close association between HDL-C and adverse cardiovascular outcomes. Traditional cognition of HDL-C has argued that it is inversely correlated with CVD or mortality, Unfortunately, as the latest evidence accumulates gradually, more doubts are raised about its protective effect. Recent studies have shown that the dose-response relationship between HDL-C levels and cause-specific mortality is not a linear correlation any more as traditionally described. It is believed that an extremely high level of HDL-C not only fails in supporting the concept of protecting the heart but even paradoxically increases cardiovascular morbidity or mortality. Furthermore, heredity studies have indicated that high HDL-C levels do not reduce the risk of myocardial infarction(MI). However, there are also some published articles implying that the relationship between HDL-C and all-cause mortality, cardiovascular death, and stroke is not significant. It is therefore that there is uncertainty about the significance of HDL-C as a clinical indicator for assessing cardiovascular risk.

METHODS

Participant or population: No limitation.

Intervention: Cohort studies were included if the research (a) assessed the association between extremely high HDL-C levels and risks of all-cause and cardiovascular death, stroke, MI, and heart failure; (b) contained relative risks (RR), hazard ratios (HR), or odds ratios (OR) of 95% confidence intervals (CI); (c) included estimates of at least three categories of HDL-C measurements in the analysis; (d) considered the normal levels of HDL-C as the reference range.

Comparator: Considered the normal levels of HDL-C as the reference range.

Study designs to be included: We will include cohort studies, prospective cohort, retrospective cohort, the following research types including case-control studies, animal experiments, irrelevant outcomes, no extremely high levels of HDL-C, duplicate publications, reviews, meta-analyses, non-English language, abstracts, letters, case reports, and articles for which the full text was not available were excluded.

Eligibility criteria: Inclusion criteriaCohort studies will be included if the research (a) assess the association between extremely high HDL-C levels and risks of all-cause and cardiovascular death, stroke, MI, and heart failure; (b) containe relative risks (RR), hazard ratios (HR), or odds ratios (OR) of 95% confidence intervals (CI); (c) include estimates of at least three categories of HDL-C measurements in the analysis; (d) consider the normal levels of HDL-C as the reference range. Exclusion criteriaThe following research types including case-control studies, animal experiments, irrelevant outcomes, no extremely high levels of HDL-C, duplicate publications, reviews, meta-analyses, non-English language, abstracts, letters, case reports, and articles for which the full text will be not available were excluded. Besides, repetitive publications with an identical cohort, including HDL-C levels reported the most abundant data, or data with a larger number of outcomes or sample sizes will be excluded.

Information sources: Embase, PubMed, Cochrane Library, and Web of Science.

Main outcome(s): Embase, PubMed, Cochrane Library, and Web of Science.

Quality assessment / Risk of bias analysis: Two authors will screen potentially relevant articles and resolve all discrepancies through discussion. Both of the described authors will apply the Newcastle-Ottawa Scale to assess the quality of included studies based on the selection of study groups, the comparability of the groups, and the ascertainment of outcomes of interest . Each study will be awarded up to

nine 9 stars, and those awarded >7 stars will be considered high quality.

Strategy of data synthesis: We will assume that the HR or OR for the risk of adverse cardiovascular outcomes is roughly the same as the RR, in the cohort study. Multivariate-adjusted RRs with 95%CI will be extracted and used for the current analysis. When heterogeneity (I2) < 50%, the combined RR and 95%CI will be estimated using a fixed-effects model; otherwise, a random-effects model is applied. The results will be stratified by sex and the data reported separately will be pooled using a fixed-effects model before inclusion in the meta-analysis. Cochran Q and I2 statistics will be applied to assess heterogeneity, and P < 0.05 will be considered the Q statistics will be statistically significant.

Subgroup analysis: Subgroup analyses will be stratified by the sex of participants and experimental design.

Sensitivity analysis: Sensitivity analysis will be performed by excluding one study at a time and assessing whether the results will be strongly influenced by a single study. Additionally, potential publication bias will be assessed using Begg's and Egger's.

Country(ies) involved: China.

Keywords: High-density lipoprotein cholesterol, Meta-analysis, cohort studies, adverse cardiovascular outcomes.

Contributions of each author:

Author 1 - Guanwei Zhang.
Email: 994524495@qq.com
Author 2 - Jiajuan GUO.
Email: gjj-2005@163.com
Author 3 - Hongguang Jin.
Email: 7420465@qq.com
Author 4 - Xiaojing Wei.
Email: 550460991@qq.com
Author 5 - Xing Zhu.
Email: 1501625356@qq.com
Author 6 - Weitao Jia.
Email: 1531989947@qq.com
Author 7 - Yongsheng Huang.
Email: lingxi1622@163.com

Support: 1.Evaluation study of Chinese medicine intervention in the rehabilitation programme for chronic heart failure (Project ref20200403102SF). Funding provided by Department of Science and Technology of JiLin Province. 2.Correlation study between Chinese medical syndrome and test data in chronic heart failure based on disease early warning(Project ref 2020094) . Funding provided by Administration of Traditional Chinese Medicine of JiLin Province.