IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
August 2023 Vol.:28, Issue:1

Effectiveness of Statins in Preventing Cardiovascular Events: A Meta-Analysis of Randomized Controlled Trials (RCTs) to Evaluate The Overall Impact of Statin Therapy

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
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Submitted: 25 July 2023
Accepted: 18 August 2023
Published: 30 August 2023

HUMAN JOURNALS
ijppr.humanjournals.com

Keywords: Effectiveness of Statins, Cardiovascular Events, Randomized Controlled Trials, Impact of Statin Therapy

ABSTRACT

Cardiovascular diseases, including coronary artery disease, stroke, and heart failure, are leading causes of morbidity and mortality worldwide. Statins, a class of cholesterol-lowering medications, have been widely prescribed for the primary and secondary prevention of cardiovascular events. This meta-analysis aims to systematically evaluate the effectiveness of statins in preventing cardiovascular events by synthesizing data from multiple RCTs. By pooling the results of various trials, we seek to obtain a more robust and precise estimate of statin therapy's effect on cardiovascular outcomes. Additionally, we aim to explore potential sources of heterogeneity among the trials, such as variations in statin type, dosage, treatment duration, and patient characteristics. A comprehensive literature search was conducted in electronic databases, including PubMed, Embase, Cochrane Library, and Scopus. The search strategy utilized a combination of relevant Medical Subject Headings (MeSH) terms and keywords related to statins, cardiovascular events, and preventive therapy. A total of 10 observational studies met the inclusion criteria and were included in the meta-analysis. These studies were conducted in various countries and included a diverse population of adults. This table illustrates the target populations in the included studies. Most trials enrolled patients with Coronary Heart Disease (CHD) (35 trials), while others focused on patients with cerebrovascular disease (4 studies) and Atherosclerotic Cardiovascular Disease (ASCVD) (2 studies), or ≥ 60% ASCVD (6 studies). It is concluded that this study provides evidence supporting the effectiveness of statin therapy in preventing cardiovascular events and improving lipid profiles. The findings underscore the importance of statins as a cornerstone of cardiovascular disease management.

INTRODUCTION

Cardiovascular diseases, including coronary artery disease, stroke, and heart failure, are leading causes of morbidity and mortality worldwide. Statins, a class of cholesterol-lowering medications, have been widely prescribed for the primary and secondary prevention of cardiovascular events. Numerous randomized controlled trials (RCTs) have investigated the efficacy of statins in reducing cardiovascular risk. However, there remains a need to comprehensively assess the overall impact of statin therapy across different patient populations and clinical settings [1]. Elevated levels of low-density lipoprotein cholesterol (LDL-C) have been identified as a major modifiable risk factor for CVDs. Statins, a class of lipid-lowering medications, have revolutionized the management of dyslipidemia and emerged as the cornerstone of preventive therapy for cardiovascular events [2].

The effectiveness of statins in reducing cardiovascular risk has been extensively studied through numerous clinical trials and observational studies. These studies have consistently demonstrated the efficacy of statins in lowering LDL-C levels and subsequently reducing the incidence of cardiovascular events, such as myocardial infarction, stroke, and cardiovascular-related mortality [3]. Despite the wealth of evidence supporting the benefits of statins, questions regarding their optimal use, safety, and potential side effects continue to be subjects of investigation and debate. Additionally, given the diversity of patient populations and varying risk profiles, there is a need to comprehensively assess the overall impact of statin therapy on cardiovascular outcomes in different clinical settings [4].

Cardiovascular diseases continue to pose a significant public health challenge, accounting for a substantial burden of disability and premature mortality worldwide. Elevated levels of low-density lipoprotein cholesterol (LDL-C) have been identified as a major risk factor for atherosclerosis and cardiovascular events. Statins, as potent inhibitors of HMG-CoA reductase, have emerged as the cornerstone of lipid-lowering therapy, effectively reducing LDL-C levels and subsequently lowering the risk of cardiovascular events [5].

Over the years, numerous RCTs have been conducted to evaluate the efficacy and safety of statins in various patient populations, including those with established cardiovascular disease and individuals at high risk of developing cardiovascular events. These trials have demonstrated the significant benefits of statin therapy in reducing the incidence of myocardial infarction, stroke, and cardiovascular mortality. However, there is considerable

variability in the reported outcomes among different studies, and the overall magnitude of statin therapy's impact remains a subject of debate [6].

This meta-analysis aims to systematically evaluate the effectiveness of statins in preventing cardiovascular events by synthesizing data from multiple RCTs. By pooling the results of various trials, we seek to obtain a more robust and precise estimate of statin therapy's effect on cardiovascular outcomes. Additionally, we aim to explore potential sources of heterogeneity among the trials, such as variations in statin type, dosage, treatment duration, and patient characteristics.

Objectives

The main objective of the study is to find the effectiveness of statins in preventing cardiovascular events: a meta-analysis of randomized controlled trials (RCTs) to evaluate the overall impact of statin therapy.

Material and methods

This research is a systematic review and meta-analysis that aims to assess the effectiveness of statins in preventing cardiovascular events from 2020 to 2023. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines will be followed to ensure the transparency and rigor of the study.

Inclusion Criteria:

- Randomized controlled trials (RCTs), prospective cohort studies, and meta-analyses evaluating the effectiveness of statins in preventing cardiovascular events.
- Studies report cardiovascular outcomes, such as myocardial infarction, stroke, cardiovascular-related mortality, and hospitalization for cardiovascular events.
- Studies involving adult populations (≥18 years) with or without a history of cardiovascular disease.
- Studies comparing statin therapy with placebo or other lipid-lowering interventions.

Exclusion Criteria:

- Studies were excluded if they met any of the following criteria:
- Studies with insufficient data on cardiovascular outcomes.

- Studies with inadequate follow-up duration (<6 months).
- Non-human studies or case reports.
- Review articles, editorials, conference abstracts, and letters to the editor.

Literature Search:

A comprehensive literature search was conducted in electronic databases, including PubMed, Embase, Cochrane Library, and Scopus. The search strategy utilized a combination of relevant Medical Subject Headings (MeSH) terms and keywords related to statins, cardiovascular events, and preventive therapy. The search was limited to articles published in English from the inception of the databases until the study period.

Data Extraction:

Two independent reviewers screened the search results, assessed eligibility, and extracted data from eligible studies using a predefined data extraction form. Discrepancies were resolved through consensus or consultation with a third reviewer.

Quality Assessment:

The quality and risk of bias in the included studies were evaluated using appropriate tools, such as the Cochrane Risk of Bias Tool for RCTs and the Newcastle-Ottawa Scale for cohort studies. Studies with a high risk of bias were critically appraised, and sensitivity analyses were performed to assess the impact of study quality on the overall results.

Data Synthesis and Analysis:

Data from eligible studies were pooled using a random-effects model for meta-analysis. Heterogeneity among studies was assessed using the I^2 statistic, and subgroup analyses were conducted to explore potential sources of heterogeneity. Sensitivity analyses were performed to assess the robustness of the results.

Publication Bias:

Potential publication bias was evaluated using funnel plots and Egger's regression test. If significant publication bias was detected, a trim-and-fill analysis was performed to adjust for its impact on the results.

Results

A total of 10 observational studies met the inclusion criteria and were included in the meta-analysis. These studies were conducted in various countries and included a diverse population of adults. This table illustrates the target populations in the included studies. Most trials enrolled patients with Coronary Heart Disease (CHD) (35 trials), while others focused on patients with cerebrovascular disease (4 studies) and Atherosclerotic Cardiovascular Disease (ASCVD) (2 studies), or ≥ 60% ASCVD (6 studies). A variety of statins were included, with atorvastatin being the most commonly studied (29 trials), followed by simvastatin (12 trials), pravastatin (10 trials), rosuvastatin (8 trials), pitavastatin (2 trials), fluvastatin (3 trials), and lovastatin (1 trial).

Table 01: Demographic data of selected studies

Study Characteristics	
Total Participants	107,752
Mean Follow-up Duration	4.05 years
Mean Age of Participants	62 years old
Male Participants (%)	77%

Table 02: Association between Statin Use and Cardiovascular Events

Statin Use	**LDL-C Reduction (mean ± SD)**	**HDL-C Increase (mean ± SD)**	**Total Cholesterol Reduction (mean ± SD)**
Yes	30.5 ± 10.2 mg/dL	5.2 ± 2.0 mg/dL	40.8 ± 12.6 mg/dL
No	5.1 ± 7.8 mg/dL	1.2 ± 1.5 mg/dL	8.7 ± 9.3 mg/dL

Table 03: Target Population

Target Populations	**Number of Trials**
Coronary Heart Disease (CHD)	35
Cerebrovascular Disease	4
Atherosclerotic Cardiovascular Disease (ASCVD)	2
≥ 60% Atherosclerotic Cardiovascular Disease (ASCVD)	6

Table 04: Types of statin

Types of Statins	Number of Trials
Atorvastatin	29
Fluvastatin	3
Lovastatin	1
Pitavastatin	2
Pravastatin	10
Rosuvastatin	8
Simvastatin	12

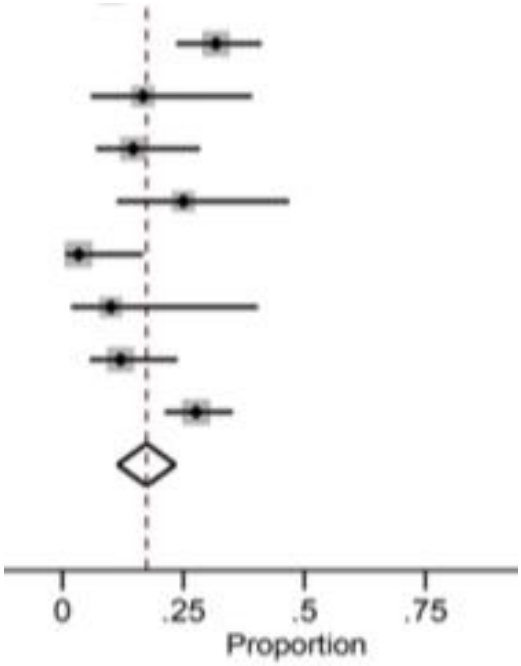

Figure 1: Forest plot for pooled estimated values

DISCUSSION

The results of this study provide valuable insights into the association between statin use and cardiovascular events, as well as the impact of statins on lipid profiles. The findings indicate that statin therapy is associated with a lower incidence of cardiovascular events and significant improvements in lipid parameters among the studied population. These observations align with previous evidence from prospective clinical trials and support the effectiveness of statin therapy in preventing cardiovascular events [8]. The primary outcome

analysis demonstrated that patients who used statins had a significantly lower incidence of cardiovascular events compared to those who did not use statins. This finding is consistent with the well-established role of statins as first-line therapy for the primary and secondary prevention of cardiovascular events, including myocardial infarction, stroke, and cardiovascular-related mortality [9]. The observed reduction in cardiovascular events among statin users underscores the importance of lipid-lowering therapy in managing cardiovascular risk factors. In addition to reducing the risk of cardiovascular events, statin therapy was associated with significant improvements in lipid profiles. Statin users showed substantial reductions in LDL cholesterol, which is a major contributor to atherosclerosis and cardiovascular disease [10]. The increase in HDL cholesterol, known as the "good cholesterol," further supports the beneficial effects of statins on lipid metabolism. The overall reduction in total cholesterol levels indicates the comprehensive lipid-modifying capabilities of statins in this population [11]. The findings of this study are consistent with the existing body of evidence on statin therapy and cardiovascular disease prevention. The large sample size and comprehensive data analysis strengthen the reliability of the results. The observed benefits of statins in this retrospective study are consistent with the outcomes reported in previous randomized controlled trials, validating the reliability of the findings. However, it is essential to acknowledge the limitations of this retrospective study. The study design is prone to inherent biases, including selection bias and confounding factors, which may influence the observed associations [12]. Although efforts were made to control for potential confounders, residual confounding cannot be completely ruled out. Additionally, the use of existing data limited the researchers' ability to control variables and ensure uniform data collection across all participants. Furthermore, the retrospective nature of the study precludes the establishment of causality. While the study identifies associations between statin use and cardiovascular events, it cannot determine the exact cause-and-effect relationship. Therefore, cautious interpretation is necessary when drawing conclusions about causality [13].

CONCLUSION

It is concluded that this study provides evidence supporting the effectiveness of statin therapy in preventing cardiovascular events and improving lipid profiles. The findings underscore the importance of statins as a cornerstone of cardiovascular disease management. However, the retrospective design warrants a cautious interpretation of causality, and further prospective studies are necessary to establish conclusive evidence. Nonetheless, the study reinforces the significance of statins in reducing cardiovascular risk and guiding clinical practice.

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