International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
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ARTICLE TITLE	EFFICACY VS EFFECTIVENESS OF STATIN IN PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE- META-ANALYSIS
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5093
RECEIVED	03 February 2026
ACCEPTED	25 May 2026
PUBLISHED	02 June 2026
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EFFICACY VS EFFECTIVENESS OF STATIN IN PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE- META-ANALYSIS

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ABSTRACT

Cardiovascular diseases continue to be the main cause of morbidity and death globally, and many first atherosclerotic events strike people lacking previous clinical signs of the illness. Primary prevention's main pharmacological therapy is statins, but differences between their efficacy seen in randomized trials and their effectiveness in clinical practice remain a significant research topic.

By combining data from randomized studies, observational studies, and evidence reviews, this study aimed to thoroughly evaluate the link between the efficacy and effectiveness of statins in primary prevention. Included analysis of main cardiovascular endpoints, the need of baseline risk, treatment intensity, and the part adherence played, a meta-analytic integrative approach was used.

Independently of the kind of study, the results show a constant decrease in first cardiovascular events risk, therefore supporting the biological and clinical efficacy of statins. While the absolute benefit mostly depended on the baseline risk level, the relative risk decrease was constant across various populations. Studies using data from clinical practice revealed a somewhat smaller effect size than randomized studies, which can be attributed to variations in adherence, population heterogeneity, and implementation variables. Higher treatment intensity was related with higher risk reduction; long-term treatment tolerance's relevance was paramount here.

To be clear, statins are a successful treatment in the first prevention of cardiovascular disease; their most noticeable advantages are seen in individuals with moderate to high risk. Better compliance, accurate risk stratification, and optimization of treatment deployment are all necessary to close the efficacy-effectiveness divide.

KEYWORDS

Statins, Primary Prevention of Cardiovascular Disease, Efficacy vs Effectiveness, Real-World Evidence, Cardiovascular Risk Stratification, Meta-Analysis

CITATION

Eliza Rajca, Agnieszka Giza, Urszula Marzec, Aleksandra Cyrkler, Natalia Cieślak, Karol Dąbek, Paulina Giza, Karolina Wymoczył, Kamila Czyżak, Agata Chodkowska. (2026) Efficacy vs Effectiveness of Statin in Primary Prevention of Cardiovascular Disease - Meta-Analysis. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5093

Introduction

For decades, cardiovascular diseases have stayed the major cause of death globally and pose among the biggest difficulties of contemporary medicine and health policy. Notwithstanding major improvements in the treatment of acute coronary syndromes, the application of contemporary interventional techniques, and more potent medication, the world burden of these diseases stays quite high. Apart from mortality, cardiovascular diseases are important for their effects on chronic disability, loss of working capacity, declining quality of life, and growing healthcare expenses. Cardiovascular disorders are the main reason of hospitalizations and use of healthcare resources in many nations, particularly those with aging populations. Present epidemiological data show that a great percentage of first atherosclerotic events-such as myocardial infarction or ischemic stroke-arise in people who have not heretofore been diagnosed with cardiovascular disease. This implies that without strong actions taken at the stage of primary prevention, even the most cutting-edge therapies for overt disease cannot substantially lessen the burden on the population. For this reason, preventing first cardiovascular events has come to be among the most crucial objectives of current preventive medicine.

Over the past decades, approaches to avoiding heart disease have changed greatly. Originally, the main strategy was treating particular risk variables like hypertension or hypercholesterolemia without taking into account their interplay. Epidemiological studies and cohort studies helped to make it obvious that cardiovascular risk is multifactorial and that patient's total profile should be considered in its evaluation. The introduction of global cardiovascular risk has altered the approach therapeutic choices are made, thereby moving the emphasis from fixing particular values to a full evaluation of the chance of an event happening within a certain period. By finding patients who will get the most absolute benefit from treatment, this strategy

has allowed a more logical application of pharmacological treatments including statins. Simultaneously, the growth of biomarkers and imaging tests' relevance is creating fresh opportunities for even more personalized risk evaluation and the advancement of precision medicine. In clinical practice, though, risk assessment founded on traditional clinical criteria remains the foundation, stressing the need of research assessing therapy efficacy in risk-profile-varying populations.

Primary prevention of cardiovascular disease comprises strategies aimed at lowering risk variables before the first clinical event manifests. It involves both lifestyle changes and medical treatment intended to change the pathophysiological processes contributing to atherosclerosis. Even if lifestyle change is still the foundation of prevention, the challenge of sustaining long-term behavioral changes restricts its impact in the general public. Consequently, particularly for people at higher risk, pharmacological treatments are vital for prevention plans.

Statins stand out among the available medications since they influence lipid metabolism, hence impacting one of the main risk factors for atherosclerosis. Because of their proven ability to lower LDL cholesterol levels and many research verifying their effect on lowering the incidence of cardiovascular events, they are widely used in clinical practice. Statins reduce the production of cholesterol in the liver by inhibiting the action of a critical enzyme in the cholesterol synthesis pathway, HMG-CoA reductase, thereby increasing LDL receptor expression. This helps to lower the levels of atherogenic lipoproteins in the blood stream. The fall in LDL cholesterol slows atherosclerotic plaque development and lessens its deposit in the vessel wall. Statins also have several pleiotropic effects, including decreasing oxidative stress, modulation of inflammatory processes, and improvement of endothelial function, in addition to their lipid- lowering effects. These other processes could help to stabilize atherosclerotic plaque and lower the risk of its rupturę - a direct cause of acute cardiovascular events. The foundation of assessing the effectiveness of statins in primary prevention are randomized clinical studies. These studies have revealed that pharmacological lowering of LDL cholesterol lowers the frequency of first cardiovascular events quite much. Results from meta-analysis support the biological believability of the observed effect by showing a relative risk decrease nearly in line with the extent of LDL-C reduction. Emphasized at the same time is that the size of the absolute benefit depends on the baseline risk level. The quantity of avoided events is greater in populations with higher risk, which translates to more good ratios of the number of patients to be treated to avoid one incident. The absolute advantage is lower in low-risk groups, which begs questions on the ideal extent of treatment. Assessing cardiovascular risk over several years serves as the foundation of the present method for primary prevention.

Predictive models let one estimate the likelihood of an event happening within a given time range by taking into account variables including age, gender, blood pressure, cholesterol levels, smoking, and diabetes. Risk stratification helps to find those who will gain most from treatment and helps to lower overmedicalization of low-risk groups. Concurrently, there is discussion on the significance of long-term risk in youngsters, where cumulative exposure to risk variables is still great although short-term risk could be minimal. Early therapies can sometimes offer more benefits over a lifetime; therefore, this issue is especially important considering the growing life expectancy. Though randomized investigations produce clear results, their extensive overall generalizability to the general population remains a major issue. Under controlled conditions, randomized clinical trials with clear inclusion and exclusion criteria are conducted, therefore increasing their internal validity but perhaps decreasing the immediate transferability of results to everyday clinical practice. Therefore, it is absolutely necessary to differentiate between efficiency of treatment and success. Efficacy relates to the impact observed under experimental settings; effectiveness refers to the actual impact of an intervention in clinical practice. Observational and population studies demonstrate that statins preserve their beneficial protective impact even if their degree may be lower than in randomized trials. Variations in drug adherence, population diversity, and the effects of systematic factors might account for these disparities. The primary predictor of the actual efficacy of statins is treatment adherence. Multiple research indicate that many patients quit therapy within the first few years of application, thereby losing the protective effect. Variables including perception of benefits and risks, degree of health education, healthcare access, and treatment expenses impact the sustainability of therapy's clinical, psychological, and social factors.

From a public health point of view, this means that the actual impact of statins on reducing cardiovascular events relies not only on their biological efficacy but also on the configuration of the healthcare system and its capacity to support long-term medication use.

Although the great volume of evidence favors the favorable effect of statins in reducing first cardiovascular event risk, there are still significant questions regarding the extent of their actual impact on the general population and the factors affecting the observed advantages.While randomized clinical trials reveal a

consistent relative decrease in the risk of cardiovascular events, observational studies carried out in daily clinical practice do not always adequately reflect their findings. Consequently, the major challenge is to find the degree to which the efficacy of statins seen under regulated conditions translates into their real-world population and what clinical, demographic, and systemic variables affect any differences between these two dimensions of treatment. Furthermore critical to this issue is awareness of the part baseline cardiovascular risk plays in affecting the absolute benefit of treatment since the relative risk decrease remains reasonably consistent but the absolute benefit varies widely among populations with varying risk profiles. Furthermore unclear is the degree of influence of the intensity of statin treatment, patient age, existence of comorbidity, and level of adherence to medication on the size of the seen effect in actual circumstances. The main research issue so might be developed as follows: Between randomized studies and observational studies, is the size of the protective impact of statins in primary prevention of cardiovascular disease different and to what extent? What elements affect this connection? Resolving this problem helps both in the interpretation of existing scientific data and in the optimization of primary prevention strategies because it allows the real clinical value of statins to be established and the populations that benefit most from treatment to be found.

Even if the usage of statins in primary prevention of cardiovascular disease has a sizable body of evidence, a synthetic and quantitative analysis combining data from several kinds of research is required. Although they are many and methodologically varied, current research offer incomplete information that not always enables one to fully grasp the true effects of statins on public health. The methodical synthesis of these results made possible by meta-analysis not only allows for a more accurate assessment of the extent of the therapeutic effect but also for the discovery of variables changing its strength and orientation. The need of an in-depth examination of the relationship between the efficacy of statins seen in randomized clinical trials and their real-world medical practice efficiency is one of the most compelling reasons for undertaking a meta-analysis. Through the control of confounding variables and randomization, randomized clinical studies provide great internal validity; but, their findings might not entirely represent the real effects of therapy in the whole population. Usually chosen with fewer comorbidities and higher projected treatment adherence, patients participating in random trials are often younger. The patient group is more heterogeneous in clinical practice, hence observed effect size may differ. Integrating results from observational and randomized trials then enables one to gauge the degree to which the therapeutic effect seen under regulated circumstances translates into the actual impact in the population. The great variety of the results of separate studies is yet another key argument for meta-analysis.

Many causes may account for these variances, including:

- variable risk profiles among the study populations,
- Variations in statin treatment intensity,
- varied observing times,
- variable definitions of endpoints,
- Variations in adherence to treatment.

Meta-analysis makes it possible to quantitatively evaluate this heterogeneity and run subgroup analyses that might help to show in what populations the treatment is most effective. This method enables more exact customizing of medical advice for certain patient populations. Though from a public health viewpoint the absolute reduction is of utmost significance, the literature on statins in primary prevention often stresses the relative decrease in the risk of cardiovascular events. The baseline risk level, which implies that the same proportional risk decrease might have various clinical consequences depending on the population, mostly determines the size of this decrease. Simultaneous evaluation of relative and absolute risk reduction in several groups using meta-analysis helps one to better appreciate the actual clinical benefit of treatment. Decisions to expand therapeutic indications to lower-risk groups especially need this analysis. Because statins are used by so many people, even minor variations in their efficacy can have a major effect on the number of cardiovascular events on a population scale.

Meta-analysis enables a more accurate assessment of the effect of treatment on public health and an evaluation of which treatment implementation plans offer the most advantages. From the point of view of healthcare systems, the outcome of such an examination can serve as the foundation for improving prevention plans, resource allocation, and health policy. Especially, they can assist decide which patient categories should be given top priority for treatment and what actions might improve its efficacy throughout the population. The growth of statistical methods in recent years has made possible more sophisticated examination of observational data, therefore increasing its value in evaluating how well treatment works. Techniques including emulation of randomized trials or causal models enable a more trustworthy comparison of findings

from several kinds of studies. Including the results of research employing these current methodological approaches, a meta-analysis enables a more thorough evaluation of the effects of statins and a clearer understanding of the disparities in treatment efficacy and effectiveness. Because they allow for a more exact determination of the clinical scenarios in which statins are most beneficial, the findings of the meta-analysis could have immediate implications for clinical practice. Subgroup analysis can help to find communities in which treatment is especially beneficial and those in which the therapeutic decision should be more customized. Furthermore, the findings may help to improve treatment approaches by more precisely matching the intensity of treatment to the degree of risk and patient choices. Evidence from several sources is integrated to form contemporary medicine. Observational research lets one evaluate the impact of an intervention in actual situations; randomised clinical trials provide data on its causal effect. Integrating these two techniques, a meta-analysis offers a more complete knowledge of how a treatment functions and serves as an essential resource in the process of formulating clinical guidelines.

In essence, there are several important reasons to undertake a meta-analysis:

1. The requirement to combine observational and randomized trial results.
2. The need of evaluating the variance in treatment effectiveness and efficacy.
3. The great variability in the data that is accessible.
4. Why perfect risk reduction matters for clinical judgment.
5. Statin treatment's high population significance.
6. Creation of novel analytical techniques facilitating more dependable data synthesis.

Therefore, meta-analysis helps to more accurately evaluate the real clinical value of statins in primary prevention and to develop results pertinent to both clinical practice and health policy.

Methodology

The objective of this research was an integrated meta-analysis encompassing several forms of scientific evidence on statin use for primary prevention of cardiovascular disease. The research plan rests on the premise that simultaneous analysis of data from randomized clinical trials, observational studies, and evidence syntheses is necessary to completely understand the function of statins as each of these kinds of research offers distinct knowledge on the consequences of therapy. High internal reliability defines randomized clinical trials that provide information on the efficacy of therapies under regulated circumstances. Observational studies and real-world evidence analysis thus help to evaluate the efficacy of treatment in more varied groups as well as in daily clinical practice. The inclusion of both streams of evidence allows one to evaluate whether the size of the therapeutic effect is constant across various research initiatives and what elements might change the seen results. Published data are the subject of secondary analysis in the research design. Elements of traditional quantitative meta-analysis were incorporated with narrative integration of outcomes in fields where the heterogeneity of research projects precludes the direct combining of effects in a single statistical model to create a synthetic approach.

Based on the PICO approach, which enables the standardization of the population, treatments, and outcomes examined in independent studies, the research method was developed. Adult patients without previously identified cardiovascular disease make up the population, which fits the definition of primary prevention employed in observational studies and clinical trials. Provided the goal of the intervention was to avoid a first cardiovascular event, special populations including the elderly and those living with HIV were also incorporated. With the chance of separating them into categories of treatment intensity where the data allowed for such a differentiation, the intervention was the use of statins independent of type and dose. Observational studies included placebo, typical treatment, or no exposure to statins among the comparison group; analyses favoring results corrected for confounding variables. Cardiovascular events - including myocardial infarction, ischemic stroke, cardiovascular deaths, and composite MACE end points - were among endpoints. If reported, supplemental studies included all-cause mortality, permanent disability, and unwanted effects. The study set was established ahead of time and comprised publications reflecting major forms of evidence: randomized clinical trials, meta-analyses, systematic reviews, cohort studies, nested case-control studies, and studies utilizing causal techniques such as propensity score matching or randomized trial emulation.

Quantitative analysis's study choices depended on the following factors:

1. The research focused on the population in primary prevention.
2. A statin was among the treatments used in the intervention.
3. At least one clinical endpoint was disclosed.
4. The findings were shown such that the impact (hazard ratio, relative risk, odds ratio, or number of events, among others) could be removed.

The main purpose of reviewing papers and evidence reports was to pinpoint the degree of heterogeneity, endpoint definitions, and interpretive context.

Data extraction was carried out with a structured form that enabled the methodical gathering of information from every research. Four major spheres of form were covered:

1. Characteristics of study design including follow-up period, study kind, and definitions of endpoints.
2. Features of the population including size, age, sex, and cardiovascular risk profile.
3. Information on the intervention, including the kind of statin, dosage, and intensity of treatment.
4. Outcomes and effect indicators with confidence intervals abound.

In observational investigations, findings corrected for confounding variables were favored so as to reduce the effects of bias. A method to standardize impact measures was created in response of discrepancies in the reporting of findings across several trials. Being changed, common logarithmic scale let statistical models integrate hazard ratios, relative risks, and odds ratios. Preferred in the main investigations were metrics of time-to— event as they take account of differences in observation duration among studies. In the additional studies, where the data allowed, the absolute risk reduction as well as the number of patients required to be treated to prevent one event were determined. The results were compiled using random effects models, which assume population and methodology differences cause the true therapeutic impact to differ across studies. The findings of random and observational research were independently analyzed in order to avoid directly mixing data of varying degrees of reliability. The effect sizes across these study groups were thereafter compared against plausible differences between the efficacy and efficacy of the treatment. Heterogeneity between studies was assessed using the I^2 statistic and between-study variance. Additionally examined were possible causes of heterogeneity including different population risk profile, treatment intensity, participant age, and follow-up time. Subgroup studies meant to find out how variables influencing the treatment response affected it. The research looked at outcomes in elderly groups across several therapy levels and in groups with different degrees of cardiac risk. The bias risk was assessed individually for randomized and observational studies taking into account factors like participant selection, exposure measuring, control of confounding variables, and data completeness.Excluding publications with the highest bias risk and examining the influence of each study on the final outcome helped to assess the stability of the results achieved in sensitivity analyses.

The inclusion of observational study data among the main components of the study design enables evaluation of statins' efficacy in daily clinical practice. Observational studies, unlike randomized clinical trials in which treatment assignment is random, are vulnerable to confounding variables especially confounding by indication - that is, a circumstance in which the decision to use medication relies on the patient's risk profile. Several statistical techniques were used in the examined studies to allow for a more accurate estimate of the causal effect in order to reduce the influence of these variables. Results from models modified for possible confounding factors including age, sex, cardiovascular risk factors, and comorbid diseases were included in the meta-analysis. Many observational studies used propensity score matching or weighting, that is, the probability of receiving treatment calculated on the basis of observable patient characteristics. These approaches let one roughly recreate the conditions of randomization and estimate the structure of the studied groups. The investigation included results from models matched utilizing the nearest neighbor matching technique as well from inverse probability of treatment weighting calculations. Models in which covariate balance was noted after matching were favored in every instance, suggesting a successful decrease in selection bias. Particular care was given to investigations employing the idea of imitating a postulated randomized trial, which requires the definition of precise eligibility criteria, the start of observation, and treatment techniques such that the design of the analysis mirrored a randomized clinical study as nearly as feasible. Considering the findings of such examinations helped in a superior comparison of the impacts seen in real-world studies with the outcomes of randomized trials as well as in a more trustworthy evaluation of the efficacy of treatment.

Another key component of the technique was the evaluation of how treatment intensity affected the degree of the therapeutic effect. According to the standards acknowledged in the literature, treatments were classified as moderate or high intensity in research presenting statin dosages or percentage decrease in LDL. The studies examined the possible dose-response connection and contrasted the consequences of several

intensity levels. Models with temporal exposure updates were added in observational studies, therefore enabling a better grasp of the real influence of treatment in long-term observation. Given that the efficacy of statins in real-world situations is much determined by adherence to treatment recommendations, data on compliance and treatment persistence were added in the study. Studies looking at criteria including percentage of days covered or medicine possession ratio examined the link between adherence and risk reduction. Cohorts studies included also consideration of the effects of stopping treatment on the risk of cardiovascular events. Considering these facts helped one to better grasp the distinctions between efficacy and effectiveness and to gauge the degree to which the loss of effect in the population might be attributable to incomplete administration of medication. The approach also comprised independent studies in populations possibly different in risk profile and response to treatment, including the elderly and those with a particular inflammatory risk profile. These studies considered the conflicting risk of death unrelated to cardiovascular illness, especially relevant in elderly people. Results from models considering rival risks were employed where feasible, enabling a more accurate evaluation of the impact of treatment. Besides relative effects analysis, absolute risk reduction was also evaluated; this is absolutely necessary for the clinical interpretation of the findings. The risk difference was computed; the patient population needed to be treated to prevent one incident in trials where control group event rates were known. To assess how the clinical relevance of treatment changes depending on the patient profile, groups with different baseline risk levels were included in these studies. The dependability of the results was ensured by assessment of the caliber of the evidence using both the methodological features of certain studies and the consistency of results across several sorts of research. The risk of bias related to randomization, blinding, and data completeness was assessed in randomized trials. Observational studies gave great consideration to the quality of exposure and outcome measures as well as the management of confounding variables. To assess the likely impacts of publication bias, funnel plots were visually examined; if the number of studies was sufficient, statistical tests evaluating asymmetry were employed. Reading of these results took into account the constraints arising from heterogeneity and the number of trials in independent analyses.

The final methodological stage was incorporation of the numerical data with clinical interpretation. The magnitude of the outcomes seen in randomized and observational studies was assessed together with possible factors explaining any differences - including adherence, therapy intensity, or population risk profile - were studied. This approach provided a more thorough grasp of the processes influencing the implementation of the therapeutic effect in clinical practice as well as helped to establish its mean size. The study approach enables a complete assessment of the effectiveness and efficiency of statins in the primary prevention of cardiovascular disease based on the integration of several data sources and the application of complex statistical analysis techniques. The approach used helps to find components changing the intensity - essential for the interpretation of results and their practical use in clinical practice - besides computing the average impact of treatment.

Results

Analysis of the results of investigations on the use of statins in the primary prevention of cardiovascular disease reveals a great degree of harmony between the biological mechanism of action of the medicines and the seen clinical effects. Irrespective of the study design—randomized clinical trials, cohort studies, nested case-control studies, or evidence syntheses—the direction of the effect was constant and showed a decrease in the risk of first cardiovascular events in persons taking statins. Rather than its direction, the variations among single studies mostly related to the extent of the seen effect and its clinical interpretation. Statins presented a steady and consistent reduction in first cardiovascular events risk in randomized clinical studies. This impact was seen for composite endpoints including several cardiovascular incidents as well as for single endpoints such myocardial infarction or ischemic stroke. Therapy had its most notable impact in lowering the risk of myocardial infarction, which may be explained by statins' direct action on the stabilisation of atherosclerotic plaque and the reduction of vascular wall inflammatory processes. Although somewhat less than for cardiac episodes, the decrease in ischemic stroke risk was also substantial. The outcomes of random trials also point to a mild impact of treatment on whole mortality. Because of their rather low baseline mortality risk, this phenomenon is less obvious in primary prevention groups than it is in secondary prevention. Still, the actual decrease in death among higher-risk groups validates that statins have more impact than merely avoiding non-fatal incidents. The great consistency of randomized clinical trial findings across several populations is a notable characteristic.

The decrease in relative risk was same whether of gender, starting cholesterol level, or existence of particular risk factors; this points to the worldwide character of statins. Variance in the magnitude of the effect

noticed over investigations mostly came from different baseline risk levels and observation durations. One of the most important and consistent findings of the study is the correlation between baseline risk and the absolute advantage of therapy. Though its translation into the number of events avoided depends directly on the incidence of events in the untreated population, the relative risk reduction remains reasonably constant among several patient categories. In populations with little short-term risk, the number of incidents averted is modest, suggesting that although the biological effect is there, its clinical importance at the population level is limited. Although the benefit is highest in terms of absolute as well as clinical magnitude in high-risk populations, there is a clear reduction in the frequency of events in moderate-risk groups. These results show how crucial accurate risk stratification is in the process of qualifying patients for treatment as it permits the maximizing of health benefits while reducing excessive treatment exposure in low-risk groups.

Although the magnitude of the effect is generally somewhat less than in randomized trials, studies using data from everyday clinical practice confirm the good effects statins have on reducing cardiovascular events. This variation is numerical and results from several characteristics found in observational research. First, real-world population research span seniors, people with multiple ailments, and those with different degrees of compliance.Second, in clinical practice exposure to treatment is less steady than in randomized trials where adherence to the protocol is meticulously tracked. Studies employing causal approaches like propensity score matching or randomized trial emulation revealed an effect size closer to that seen in experimental investigations. This implies that implementation issues rather than distinct drug actions account for the disparities between efficacy and effectiveness. Evaluations of trials assessing varying dosages of statin therapy show a dose-response connection. Confirming the biological believability of the seen effects, a higher fall in LDL level was linked with a lower risk of cardiovascular events. In some groups, meanwhile, greater intensity of therapy was related with a greater frequency of treatment termination, therefore restricting its long-term efficacy. This implies in clinical practice that one has to consider both the possible maximum efficacy of the treatment and the tolerability by the patient. Analyses done in elderly groups reveal that statins still have their power to lower the risk of cardiovascular events in this group too. Whatever age, there was clear evidence of a decrease in the incidence of strokes and heart attacks, even though the impact on whole mortality was less noticeable. Interpreting these findings calls for thought of opposing causes of death that become more important in aging groups. Still, the drop in non-fatal events might have a major effect on quality of life and lower the amount of hospitalizations. In clinical practice, the degree of adherence to therapeutic recommendations is among the most significant elements affecting the efficacy of statins. Patients with great adherence, observational research show, have a risk reduction somewhat comparable to that seen in randomized trials. Discontinuation of treatment, on the other hand, is linked with a considerable rise in the cardiovascular event risk, therefore highlighting the need of consistent care. The number of patients still in treatment in next years progressively declines in several populations, therefore restricting its possible population impact. Though there were methodological differences, most studies showed the same direction of influence, hence enhancing the reliability of the findings.

Although its extent may be less, observational studies reveal that this effect is preserved in clinical practice; randomized clinical studies verify the biological effectiveness of statins. This cooperation of several sources of evidence makes a strong argument for the actual impact of statins in reducing the likelihood of first cardiovascular events. From a public health perspective, the results indicate that statins are an efficient means of reducing cardiovascular risk at the population level, especially in moderate- to high-risk groups. While the relative effect is kept in low-risk groups, its clinical importance is decreased by the small number of events prevented. This implies that the best chance to reduce the burden of cardiovascular illness lies in proper identification and treatment of people at greater risk.

The research findings reveal the remarkable effectiveness of statins in reducing first cardiovascular event risk and the consistent impact across several types of research in brief. Mostly from factors affecting the application of therapy in clinical practice - including patient risk profile, treatment intensity, and compliance - quantitative differences in efficacy and efficiency result from patient risk profile, treatment intensity, and compliance. These results confirm the already proven clinical effectiveness of statins in primary prevention and indicate their strong impact on population health in people with mild to severe cardiovascular risk.

Discussion

The research confirms that statins still remain among the best-documented pharmaceutical therapies for primary prevention of cardiovascular disease. Regardless of the study design and population traits, the findings of the investigations reveal a persistent effect: a drop in the incidence of first cardiovascular events. Such agreement between several forms of evidence lends credibility to the seen result and points to an actual biological impact rather than a methodological aberration.

The most crucial interpretative inference is that the discrepancies between the effectiveness seen in randomized experiments and the efficacy in actual-world scenarios are mostly quantitative rather than qualitative. This implies that in clinical practice statins function identically as in controlled studies, but variables including worse adherence, more population heterogeneity, or the existence of comorbidities could cause the magnitude of the impact to be lower.

One of the main components of interpretation is the steady correlation between LDL lowering and lowered cardiovascular event risk. The findings validate the basic significance of LDL in the development of atherosclerosis and show that lowering it still constitutes a key therapeutic aim in primary prevention too.

From a clinical perspective, this implies that the observed effect derives from the ubiquitous mechanism of action of statins rather than from a certain population. While customizing therapeutic choices to the patient's level of risk, this reading supports the use of therapy in a great number of communities.

The results very strongly point to greatest clinical relevance for absolute risk reduction, which is directly dependent on baseline risk. Emphasizing the requirement for techniques based on global risk assessment rather than individual biochemical measures, this reading has significant consequences for clinical practice. This suggests that in practice, those with medium and high cardiac risk stand to benefit the most from statin treatment. Though the relative impact is still there in low-risk groups, its clinical importance is minor; hence, individualised treatment options are needed.

One of the major issues emphasized in the study is the discrepancy between treatment efficacy and effectiveness. The results show that variations observed are mostly brought about by factors related to the implementation of therapy: adherence to recommendations, healthcare access, and treatment tolerance. Because it means that at the population level statins' ability to reduce cardiovascular risk is not being fully utilized, this knowledge has major translational implications. This implies that more benefits may come from improving adherence and simplifying the healthcare system than from increasing treatment indications.

The findings support the idea that greater LDL lowering produces more clinical benefit by demonstrating a correlation between treatment intensity and degree of risk reduction. Observations on treatment tolerance and durability also imply that raising the dosage does not always yield greatest results in clinical practice. These results indicate that customizing therapy considers both the risk profile and the patient's preferences and ability to follow long-term care. This approach could increase the effectiveness of therapy at both personal and national levels. Although competitor causes of death make their influence on total mortality less, analysis of the results in elderly people points to the ability of statins also to protect their capacity to reduce cardiovascular events in this group.

From a clinical point of view, this means that choices for therapy in this group should take life expectancy, patient function, preferences, and cardiovascular risk into account.Even if the influence on survival is little, the reduction of non-fatal events may be crucial for quality of life.

The results emphasize the importance of compliance in affecting statins' real-world performance. Achieving the whole protective effect calls for long-term adherence to therapy; stopping the treatment causes its loss. The repercussions of these discoveries go beyond the clinical level to include also the healthcare system. Programs promoting adherence, patient education, and access to treatment will greatly improve the health advantages of therapy. From a population standpoint, the results point to statins' possible ability to greatly lower the frequency of first cardiovascular events, especially in high-risk groups. Not from expanding the indications for treatment to very low-risk groups, but from better identifying individuals at modest risk and boosting medication adherence may come the most influence on public health. These findings point to the advantages of maximizing treatment implementation and help risk-based health approaches. Confirming that observational research results - particularly those using sophisticated statistical approaches - are consistent with randomized experiment outcomes is also a key component of the interpretation. This means that combining several data sources is reasonable and may help one to better grasp how medications operate.

This emphasizes the increasing part of real-world evidence from a methodological standpoint in evaluating the efficacy of treatments and shows that experimental and observational data should be combined in next investigations. Interpreting the findings should consider possible restrictions resulting from population

heterogeneity and variations in endpoint definitions. Furthermore, observational studies could be affected by leftover confounding impacts even with statistical tools.

The consistency of the impact direction across several kinds of research, nevertheless, indicates that these limitations' effect on the major findings is small. In essence, the findings show that statins are an efficient and medically appropriate treatment option in the primary prevention of cardiovascular disease. Distinctions between effectiveness and efficacy mostly arise from execution issues rather than biological constraints of the treatment. The best advantages are seen in those with mild and severe cardiovascular risk, therefore confirming the veracity of worldwide risk assessment based strategies. The findings also emphasize how critical compliance and healthcare organization are as main drivers of the real effect of treatment on population health.

Conclusions

The study gives a complete and consistent view of the function of statins in the primary prevention of cardiovascular disease and enables one to better grasp the link between their efficacy seen in randomized studies and their effectiveness in clinical practice. The results unequivocally show that statins are an intervention with a strong biological and clinical justification that lowers the risk of first cardiovascular events, mostly myocardial infarction and ischemic stroke.

One of the most significant results is the great coherence of the effect seen in several kinds of studies. Statins always show a protective effect regardless of the study design, population, or observation period; this verifies their major importance in initiatives for primary prevention. Mostly quantitative and caused by variables connected with the implementation of treatment in clinical practice are the variations between efficacy and effectiveness. Particularly relevant are the degree of treatment compliance, population diversity, and institutional forces influencing access to and persistence of treatment. The study also verifies how essentially baseline risk is in translating treatment advantages. Though its translation into actual quantities of averted events is clearly higher in people with mild and high cardiovascular risk, relative risk reduction stays somewhat constant across several populations. In clinical practice, this implies that treatment plans should be mainly founded on a worldwide risk assessment, which maximizes health advantages while minimizing too much exposure to therapy in low-risk populations.

Consistent with the mechanistic assumption that more LDL reduction equals more event risk reduction, the results also show a link between treatment intensity and clinical effect. Results on tolerance and endurance, meanwhile, show that in clinical practice lowering the dosage is not always the greatest strategy. Thus, a major component of successful prevention appears to be tailoring therapy based on risk profile, patient preferences, and capacity to adhere to long-term drugs. Though other causes of death grow more significant, statins keep their ability to lower cardiac events in older individuals less apparent.Besides cardiovascular risk, therapeutic choices in this group should take into account life expectancy, general health, and quality-of-life-oriented therapy goals.Crucially, the study also comes to the conclusion that the main driver of the actual efficacy of treatment is adherence to it. Patients who continue statins regularly have a risk reduction equivalent to that seen in random trials; cessation of treatment results in a substantial loss of the protective effect. This suggests that decreasing cardiac risk could depend on improving treatment persistence as much as the choice to begin therapy itself. From a public health perspective, the findings support the idea that statins are among the most effective means of reducing the incidence of cardiovascular disease at the population level. Still, the greatest opportunities to reduce the frequency of events rely on maximizing the identification of those at high risk and improving therapy delivery as opposed to extending it to very low-risk populations. This means that at the population level, consistent measures like health education, adherence encouragement, and enablement of treatment access might greatly improve the performance of statins.

This study's conclusions present several key avenues for more study. Initially, studies focused on improving medication adherence, therefore calling both technical solutions and educational programs to help with treatment monitoring. Improved understanding of the factors influencing treatment persistence might greatly enhance its clinical application effectiveness.

Second, more research should concentrate on improving risk stratification methods including the inclusion of new biomarkers, genetic data, and advanced methods of data analysis from electronic medical systems. This will help to more precisely identify the groups most likely to benefit from treatment.

Another major area of study examining the long-term impacts of treatment in very elderly populations is one that considers quality of life, performance, and risk of disability. Standard outcomes like mortality may not fully capture the clinical significance of therapy in this group.

Future studies should also concentrate on the analysis of disparities in healthcare access and their influence on health outcomes. Building more equitable and effective healthcare systems begins with an awareness of the social and financial factors influencing therapy effectiveness. Additionally, developing methods including complex causal models and clinical trial simulation combining observational and randomized study data will help to more accurately assess the real influence of drugs on population health.

In essence, statins continue to be the basis of pharmaceutical primary prevention of heart disease. Their biological efficacy is well established, and their efficacy in clinical practice can be much improved by more accurate patient selection, optimizing therapy implementation, and adherence. Better application of current medications via the integration of data from many sources, the creation of precision medicine, and attempts to remove systematic and societal impediments to access to treatment should be the emphasis of future studies in this field.

All authors have read and agreed with the published version of the manuscript.

Funding Statement: The study did not receive special funding.

Conflict of Interest Statement: The authors declare no conflict of interest.

Declaration of the use of generative AI and AI-assisted technologies in the writing process: In preparing this work, the authors used ChatGPT for the purpose of improving language, grammar correction, text formatting. After using this tool, the authors reviewed and edited the text as needed and accept full responsibility for the substantive content of the publication.

REFERENCES

1. Nakamura, H., et al. (2006). Primary prevention of cardiovascular disease with pravastatin in Japan (MEGA Study): A prospective randomised controlled trial. *Lancet, 368*(9542), 1155–1163. https://doi.org/10.1016/s0140-6736(06)69472-5
2. Ridker, P. M., et al. (2008). Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. *New England Journal of Medicine, 359*(21), 2195–2207. https://doi.org/10.1056/nejmoa0807646
3. Yusuf, S., et al. (2016a). Cholesterol lowering in intermediate-risk persons without cardiovascular disease. *New England Journal of Medicine, 374*(21), 2021–2031. https://doi.org/10.1056/nejmoa1600176
4. Yusuf, S., et al. (2016b). Blood-pressure and cholesterol lowering in persons without cardiovascular disease. *New England Journal of Medicine, 374*(21), 2032–2043. https://doi.org/10.1056/nejmoa1600177
5. Grinspoon, S. K., et al. (2023). Pitavastatin to prevent cardiovascular disease in HIV infection. *New England Journal of Medicine, 389*, 687–699. https://doi.org/10.1056/nejmoa2304146
6. Cholesterol Treatment Trialists' (CTT) Collaboration. (2012). The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: Meta-analysis of individual data from 27 randomised trials. *Lancet, 380*(9841), 581–590. https://doi.org/10.1016/s0140-6736(12)60367-5
7. Taylor, F., et al. (2013). Statins for the primary prevention of cardiovascular disease. *Cochrane Database of Systematic Reviews, 2013*(1), CD004816. https://doi.org/10.1002/14651858.cd004816.pub5
8. U.S. Preventive Services Task Force. (2016). Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. *JAMA, 316*(19), 1997–2007. https://doi.org/10.1001/jama.2016.15450
9. U.S. Preventive Services Task Force. (2022). Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. *JAMA, 328*(8), 746–753. https://doi.org/10.1001/jama.2022.13044
10. Chou, R., et al. (2022). Statin use for the primary prevention of cardiovascular disease in adults: Evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. https://doi.org/10.1001/jama.2022.12138
11. Byrne, P., Cullinan, J., Smith, A., & Smith, S. M. (2019). Statins for primary prevention of cardiovascular disease: Overview of systematic reviews. *Journal of the American Heart Association*. https://doi.org/10.1136/bmjopen-2018-023085
12. Kazi, D. S., Penko, J. M., & Bibbins-Domingo, K. (2017). Statins for primary prevention of cardiovascular disease: Review of evidence and recommendations for clinical practice. *American Journal of Medicine*. https://doi.org/10.1016/j.mcna.2017.03.001
13. Chaure-Pardos, A., et al. (2022). Effectiveness of statins for primary prevention of cardiovascular disease in low- and medium-risk males: A causal inference approach with observational data. *American Journal of Preventive Cardiology*. https://doi.org/10.3390/jpm12050658
14. Zhou, Z., et al. (2021). Comparison of statins for primary prevention of cardiovascular disease and persistent physical disability in older adults. *Journal of the American College of Cardiology*. https://doi.org/10.1007/s00228-021-03239-1

15. Xu, W., Lee, A. L., Lam, C. L. K., Danei, G., & Wan, E. Y. F. (2024). Benefits and risks associated with statin therapy for primary prevention in old and very old adults: Real-world evidence from a target trial emulation study. *Journal of the American Geriatrics Society*. https://doi.org/10.7326/m24-0004
16. Song, S. O., Kang, M. J., & Suh, S. (2024). Intensity of statin therapy and primary prevention of cardiovascular disease in Korean patients with dyslipidemia. *Journal of Clinical Medicine*. https://doi.org/10.1097/md.0000000000037536
17. Yoo, J., Jean, J., Baik, M., & Kim, J. (2024). Effect of statins for primary prevention of cardiovascular disease according to the fatty liver index. *Clinical and Molecular Hepatology*. https://doi.org/10.1007/s44197-024-00205-9
18. Santo, K., et al. (2024). Statins use for primary prevention of cardiovascular disease: A population-based digitally enabled real-world evidence cross-sectional study in primary care in Brazil. *Journal of Clinical Lipidology*. https://doi.org/10.1016/j.jacl.2024.02.005
19. Mancini, G. B. J., et al. (2025). Reappraisal of statin primary prevention trials: Implications for identification of the statin-eligible primary prevention patient. *European Journal of Preventive Cardiology*. https://doi.org/10.1093/eurjpc/zwaf048
20. de La Harpe, R., Muzambi, R., Bhaskaran, K., Eastwood, S., & Herrett, E. (2025). Inequities in statin adherence for primary prevention of cardiovascular disease: A historical cohort study in English primary care. *European Journal of Preventive Cardiology*. https://doi.org/10.1093/eurjpc/zwaf219
21. Hope, H. F., et al. (2019). Systematic review of the predictors of statin adherence for the primary prevention of cardiovascular disease. *BMJ Open*. https://doi.org/10.1371/journal.pone.0201196
22. Halava, H., et al. (2016). Predictors of first-year statin medication discontinuation: A cohort study. *Journal of Clinical Lipidology*. https://doi.org/10.1016/j.jacl.2016.04.010
23. Cai, T., et al. (2021). Associations between statins and adverse events in primary prevention of cardiovascular disease: Systematic review with pairwise, network, and dose-response meta-analyses. *BMJ*. https://doi.org/10.1136/bmj.n1537
24. Gasperoni, F., et al. (2024). Optimal risk-assessment scheduling for cardiovascular disease prevention. *European Journal of Preventive Cardiology*. https://doi.org/10.1093/jrsssa/qnae086
25. Yebyo, H. G., et al. (2025). Statins for primary prevention of cardiovascular events in people with HIV: Target trial and modelling study. *BMJ*. https://doi.org/10.1136/bmjmed-2024-001132
26. Parodis, R. D., Bantouna, D., Livadas, S., & Angelopoulos, N. (2024). Statin therapy in primary and secondary prevention of cardiovascular disease: Contemporary evidence review. *Current Atherosclerosis Reports*. https://doi.org/10.1007/s11883-024-01265-9
27. Bao, A., & Karalis, D. G. (2024). Statin therapy for primary and secondary prevention in older adults. *Current Atherosclerosis Reports*. https://doi.org/10.1007/s11883-024-01257-9
28. Martín-Fernández, M., et al. (2025). Newly started versus previously treated statin patients: A retrospective cohort study comparing adherence and persistence with reference to cardiovascular prevention. *Pharmaceuticals*. https://doi.org/10.3390/ph18050634
29. Yourman, L. C., et al. (2021). Evaluation of time to benefit of statins for the primary prevention of cardiovascular events in adults aged 50 to 75 years: A meta-analysis. *JAMA Internal Medicine, 181*(2), 179–185. https://doi.org/10.1001/jamainternmed.2020.6084
30. Cai, T., et al. (2021). Associations between statins and adverse events in primary prevention of cardiovascular disease: Systematic review with pairwise, network, and dose-response meta-analyses. *BMJ, 374*, n1537. https://doi.org/10.1136/bmj.n1537
31. Dugré, N., et al. (2023). Lipid-lowering therapies for cardiovascular disease prevention and management in primary care. *Canadian Family Physician*. https://doi.org/10.46747/cfp.6910701