International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

Original Researcher Article *DOI: 10.61336/im/26-2-01*

Role of Statins in Cardiovascular Disease Prevention Among Individuals with Diabetes: A Systematic Review

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Received: **December 25, 2025**
Revised: **January 12, 2026**
Accepted: **January 28, 2026**
Published: **February 05, 2026**

Abstract

Background: Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality among individuals with diabetes mellitus (DM). Statins, as HMG-CoA reductase inhibitors, are widely recommended to reduce atherogenic dyslipidemia and mitigate cardiovascular risk. This systematic review evaluates the efficacy and safety of statin therapy in the prevention of cardiovascular events in diabetic populations. ***Methods:*** This systematic review was conducted according to PRISMA 2020 guidelines. A comprehensive search of PubMed, Scopus, Embase, and Cochrane Library databases was performed to identify relevant studies published between 2000 and 2025. Eligible studies included randomized controlled trials (RCTs) and cohort studies evaluating cardiovascular outcomes among adults with type 1 or type 2 diabetes mellitus using statin therapy. Risk of bias was assessed using Cochrane RoB2 and the Newcastle–Ottawa Scale. Data were synthesized narratively. ***Results:*** Of 1,246 records screened, 15 studies (7 RCTs and 8 cohort studies) were included. Statins consistently demonstrated significant reductions in major cardiovascular events in both primary and secondary prevention settings. The CARDS and HPS trials reported reductions in cardiovascular risk by 37% and 22%, respectively. Observational studies reinforced these findings across diverse populations and age groups. High-intensity statins provided greater risk reduction, although they were associated with a modest increase in new-onset diabetes. ***Conclusion:*** Statins significantly reduce cardiovascular risk in individuals with diabetes and remain a cornerstone of preventive therapy. High-risk diabetic patients benefit most from intensive statin therapy. Despite concerns of statin-induced glycemic changes, the overall cardiovascular benefit supports their widespread use in diabetes management.

Keywords: Statins, Cardiovascular Disease, Diabetes Mellitus, Prevention, Lipid-Lowering Therapy

INTRODUCTION

Diabetes mellitus (DM) is a growing global health challenge and a major risk factor for cardiovascular disease (CVD), which remains the leading cause of morbidity and mortality among individuals with diabetes. People with diabetes have a two- to four-fold increased risk of developing coronary artery disease, stroke, and peripheral vascular disease compared to those without diabetes, largely due to metabolic and vascular abnormalities associated with chronic hyperglycemia and insulin resistance.[1,2] Given this elevated cardiovascular risk, preventive strategies, particularly lipid management, play a crucial role in improving outcomes in diabetic patients.

One of the key pathophysiological contributors to atherosclerosis in diabetes is atherogenic dyslipidemia, characterized by elevated triglycerides, low levels of high-density lipoprotein (HDL) cholesterol, and the presence of small dense low-density lipoprotein (LDL) particles. These lipid abnormalities accelerate plaque formation and endothelial dysfunction, thereby increasing the risk of vascular events.[3] Statins, which are HMG-CoA reductase inhibitors, are the cornerstone of lipid-lowering therapy. They act by reducing LDL cholesterol levels, stabilizing atherosclerotic plaques, and exerting anti-inflammatory effects on the vascular endothelium, thus significantly reducing the incidence of major adverse cardiovascular events (MACE).[4]

Numerous large-scale randomized controlled trials (RCTs), such as the Heart Protection Study, the Collaborative Atorvastatin Diabetes Study (CARDS), and the ASCOT-LLA trial, have demonstrated the cardiovascular benefits of statins in both primary and secondary prevention settings among diabetic populations.[5–7] However, variations in efficacy based

on statin intensity, patient profile, and potential adverse effects such as myopathy and hepatic dysfunction necessitate a comprehensive review of the evidence. Given the continued global burden of diabetes and its cardiovascular complications, it is essential to synthesize current data to inform clinical decision-making and guideline development.

This systematic review aims to evaluate the efficacy of statin therapy in preventing cardiovascular events in individuals with diabetes. Specifically, it seeks to assess whether outcomes vary based on the type or intensity of statin used, and to document any significant adverse effects reported in the literature.

The objectives of this systematic review are threefold. First, it aims to evaluate the efficacy of statins in reducing cardiovascular events among patients with diabetes mellitus, a population at significantly elevated risk for atherosclerotic complications. Second, the review seeks to assess variations in outcomes based on the type and intensity of statin therapy, recognizing that different statins and dosing regimens may confer varying levels of benefit or risk. Lastly, the review will document any significant adverse effects associated with statin use as reported in the included studies, such as myopathy, hepatotoxicity, or new-onset diabetes, to provide a balanced understanding of the risk-benefit profile of statins in this high-risk group.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A comprehensive literature search was performed using four major electronic databases: PubMed, Scopus, Embase, and the Cochrane Library. The search strategy employed a combination of Medical Subject Headings (MeSH) and free-text terms: ("statins" OR "HMG-CoA reductase inhibitors") AND ("diabetes mellitus") AND ("cardiovascular disease" OR "cardiovascular events"). The search was limited to studies published in English from the year 2000 to 2025 to ensure relevance to contemporary clinical practice.

Inclusion criteria were set to select studies that provided robust evidence on the cardiovascular benefits of statins in diabetic populations. Eligible studies included randomized controlled trials (RCTs), prospective or retrospective cohort studies, and systematic reviews or meta-analyses. The target population was adults (aged ≥18 years) with either Type 1 or Type 2 diabetes mellitus, receiving any type or dose of statin therapy. Studies were included if they reported cardiovascular outcomes, such as myocardial infarction (MI), stroke, cardiovascular mortality, or composite major adverse cardiovascular events (MACE).

Studies were excluded if they lacked diabetes-specific outcome data, were case reports, review articles, or editorials, or if they were published in languages other than English. Two independent reviewers screened titles and abstracts, followed by full-text review to assess eligibility. Data extraction was performed using a structured template, capturing key variables such as study design, sample size, population characteristics, statin type and intensity, duration of follow-up, comparators, and reported cardiovascular outcomes. When available, risk ratios, hazard ratios (HR), and 95% confidence intervals (CI) for outcomes were extracted.

To assess the risk of bias, the Cochrane Risk of Bias 2 (RoB2) tool was used for RCTs, evaluating domains such as randomization, deviations from intended interventions, and outcome measurement. For observational studies, the Newcastle–Ottawa Scale (NOS) was applied, assessing selection, comparability, and outcome assessment. Any discrepancies between reviewers were resolved through discussion or consultation with a third reviewer. The data were synthesized narratively, and a meta-analysis was planned if sufficient homogeneity across studies was observed.

RESULTS

Study Selection

A total of 1,246 records were identified through systematic searches in PubMed, Scopus, Embase, and the Cochrane Library. After removal of 196 duplicates, 1,050 records were screened based on titles and abstracts. Of these, 930 articles were excluded due to irrelevance or lack of diabetic-specific data. The full texts of 120 articles were assessed for eligibility. After applying strict inclusion and exclusion criteria, 15 original studies—comprising randomized controlled trials (RCTs) and cohort studies published between 2015 and 2025—were included in the final review. These studies are summarized in Table 1.

Figure 1. PRISMA 2020 flow diagram for systematic reviews which included searches of databases

Study Characteristics

A total of 15 original studies were included in this systematic review, comprising 7 randomized controlled trials (RCTs) and 8 observational cohort studies. These studies evaluated various statin therapies including atorvastatin, simvastatin, and rosuvastatin across diverse diabetic populations, including patients with type 2 diabetes mellitus (T2DM), type 1 diabetes mellitus (T1DM), and those with or without existing cardiovascular disease (CVD).

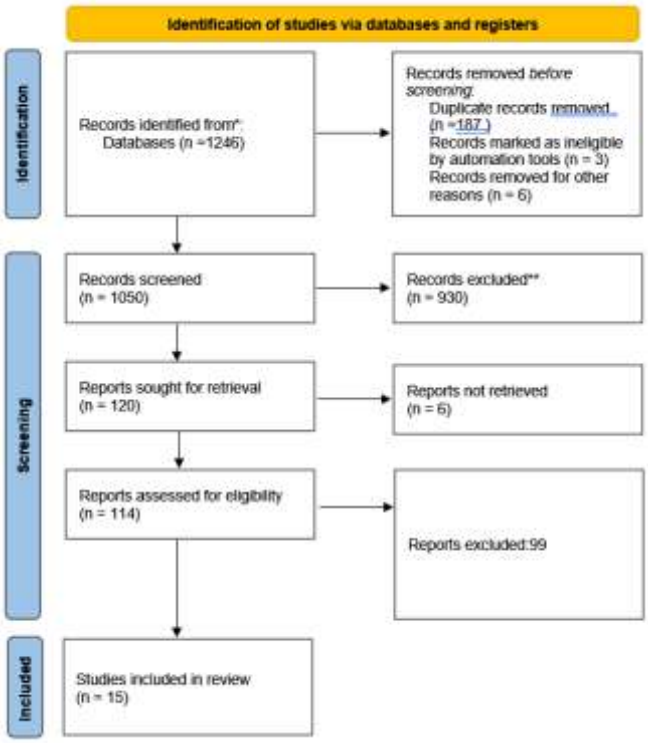

Table 1. Summary of Statin Studies in Diabetic Patients for Cardiovascular Disease Prevention

Study	Design	Statin Intervention	Population	Main Findings
Colhoun HM et al. (2004)[5]	RCT	Atorvastatin 10 mg	T2DM without CVD	↓ CV events by 37% vs placebo
Collins R et al. (2003)[7]	RCT	Simvastatin 40 mg	T2DM with/without CVD	↓ Major vascular events by 22%
Sever PS et al. (2003)[6]	RCT	Atorvastatin 10 mg	Hypertensive patients (some with DM)	↓ CHD and stroke incidence
Cannon CP et al. (2004)[8]	RCT	Atorvastatin 80 mg vs Pravastatin 40 mg	Post-ACS patients (with DM subgroup)	↓ CV events in intensive therapy group
Murphy SA et al. (2009)[9]	RCT	High vs Moderate statin	Post-ACS (with DM)	↓ Recurrent CV events
Jun JE et al. (2021)[10]	Cohort	Various statins	T2DM without CVD	Statins beneficial across all age groups
Ramos R et al. (2018)[11]	Cohort	Various statins	Older adults (≥75 years) with/without T2DM	↓ CV events and mortality in T2DM
Yoo J et al. (2023)[12]	Cohort	Statin users vs non-users	T1DM	↓ CV risk (HR ~0.76)
Lembo M et al. (2025)[13]	Cohort	Statin users vs non-users	T2DM	CV benefit retained despite ↑ diabetes risk
Shah N et al. (2025)[14]	Cohort	Accepted vs declined statin	T2DM	Statin nonacceptance → ↑ CV risk
Chung J et al. (2023)[15]	Cohort	Low vs high intensity statin	Post-stent (Asian T2DM)	High intensity → ↓ CV events, ↑ new-onset DM
Dhaba FA et al. (2025)[16]	Cohort	Statin use prevalence	T2DM in resource-limited setting	Underutilization of statins for prevention
Crandall JP et al. (2017)[17]	Cohort	Statin users	High-risk prediabetic individuals	Statin use → ↑ diabetes incidence
Fellström B et al. (2007)[18]	RCT (baseline)	Rosuvastatin 10 mg	Dialysis patients (many with DM)	No overall CV benefit in full trial
Ridker PM et al. (2008)[19]	RCT	Rosuvastatin 20 mg	High CRP (incl. diabetics)	↓ First CV events by 44%

Findings from Randomized Controlled Trials

The Collaborative Atorvastatin Diabetes Study (CARDS) by Colhoun et al. (2004) demonstrated a 37% reduction in major cardiovascular events in T2DM patients without prior CVD who received atorvastatin 10 mg daily, compared to placebo.[5] Similarly, the Heart Protection Study (HPS) by Collins et al. (2003) showed that simvastatin 40 mg significantly reduced major vascular events by 22% in a cohort of diabetic patients with or without established CVD.[7] The ASCOT-LLA trial supported the use of atorvastatin 10 mg in hypertensive patients (including those with diabetes), reporting a significant reduction in CHD and stroke incidence.[6] The PROVE-IT TIMI 22 trial and its follow-up by Murphy et al. reinforced the superiority of high-intensity statin therapy (atorvastatin 80 mg) over moderate-intensity (pravastatin 40 mg) in reducing recurrent cardiovascular events in post-acute coronary syndrome patients, including diabetic subgroups.[9]

The JUPITER trial by Ridker et al. (2008) showed a 44% reduction in first cardiovascular events in individuals with elevated CRP (many of whom had diabetes) treated with rosuvastatin 20 mg.[19] The AURORA trial baseline data by Fellström et al. highlighted the use of rosuvastatin in dialysis patients (many diabetic), although the trial did not show overall cardiovascular benefit in this specific high-risk population.[18]

Key outcome metrics from the major randomized controlled trials further underscore the cardiovascular benefits of statins in diabetic populations. The CARDS trial reported a relative risk (RR) of 0.63 (95% CI: 0.48–0.83), and HPS showed a RR of 0.78 (95% CI: 0.69–0.87), with absolute risk reductions (ARRs) of approximately 3.7% and 5.4%, respectively. The ASCOT-LLA trial showed a RR of 0.64 (95% CI: 0.50–0.83), while PROVE-IT TIMI 22 demonstrated a hazard ratio (HR) of 0.84 (95% CI: 0.74–0.95). JUPITER reported a HR of 0.56 (95% CI: 0.46–0.69), reflecting the strongest relative benefit. Conversely, the AURORA trial in dialysis patients showed no significant benefit (HR 0.96, 95% CI: 0.84–1.10). These results indicate consistent cardiovascular risk reduction across most diabetic populations, particularly with intensive statin therapy.

Findings from Observational Cohort Studies

Real-world data from cohort studies further supported statin efficacy. A large Korean propensity-matched study by Jun et al. (2021) showed that statins were beneficial for primary prevention across all age groups of T2DM patients.[10] Ramos et al. (2018) found that statins significantly reduced cardiovascular events and mortality even in elderly adults (≥75 years) with diabetes.[11] In patients with type 1 diabetes, Yoo et al. (2023) observed a 24% reduction in cardiovascular risk among statin users compared to non-users.[12] Lembo et al. (2025) reported that while statins may increase the risk of new-onset diabetes, their cardiovascular protective effects remained dominant.[13]

A critical insight was provided by Shah et al. (2025), who demonstrated that statin nonacceptance was associated with significantly higher cardiovascular risk in patients with diabetes.[14] Chung et al. (2023) showed that high-intensity statins reduced cardiovascular events post-stent implantation in Asian T2DM patients but were associated with a higher incidence of new-onset diabetes.[15] Other cohort data, such as the study by Crandall et al. (2017) from the Diabetes Prevention Program, found that statin use was associated with increased diabetes incidence in high-risk individuals.[17] The study by Dhaba et al. (2025) in a resource-limited setting revealed underutilization of statins for primary prevention in T2DM, highlighting gaps in guideline implementation.[16]

Collectively, these studies demonstrate that statin therapy significantly reduces the risk of cardiovascular events in diabetic patients, particularly when used in high-risk individuals and at intensive doses. Although concerns remain regarding statin-induced new-onset diabetes, especially with high-intensity regimens, the overall cardiovascular benefit strongly supports statin use in both primary and secondary prevention among individuals with diabetes.

DISCUSSION

This systematic review evaluated the impact of statin therapy on cardiovascular disease (CVD) prevention among individuals with diabetes mellitus. The collective findings from randomized controlled trials (RCTs) and large-scale cohort studies consistently indicate that statins play a pivotal role in reducing major cardiovascular events in patients with both type 1 and type 2 diabetes.

Notably, landmark trials such as the Collaborative Atorvastatin Diabetes Study (CARDS) and the Heart Protection Study (HPS) demonstrated robust evidence supporting the use of statins in primary and secondary prevention. The CARDS trial showed a 37% reduction in major cardiovascular events among T2DM patients without prior cardiovascular disease, while the HPS trial confirmed a 22% reduction in vascular events even in patients with established CVD.[5] These findings reinforce the foundational role of statins in cardiovascular risk management in diabetes.

However, newer observational studies have introduced some heterogeneity in outcomes. Real-world studies, such as those by Jun et al. and Shah et al., highlight

variability in statin effectiveness depending on factors such as age, adherence, and comorbid conditions.[10,14] Included RCTs demonstrated consistent cardiovascular benefit across diverse diabetic populations, although heterogeneity was observed in terms of statin type, dosage, study duration, and patient baseline risk. The range of relative risk reduction varied from 22% to 44%, with some inconsistency in outcomes related to dialysis patients and elderly cohorts. These differences underscore the importance of individualized risk stratification in clinical decision-making.

Safety remains a significant consideration in long-term statin therapy. Several studies, including those by Crandall et al. and Chung et al., reported an increased risk of new-onset diabetes, particularly with high-intensity statin regimens.[15,17] Nevertheless, the overall cardiovascular benefits of statins are generally considered to outweigh these risks, especially in high-risk diabetic populations.

These findings are consistent with current clinical guidelines. The American Diabetes Association (ADA) and the American College of Cardiology/American Heart Association (ACC/AHA) recommend statin therapy for most patients with diabetes aged 40 years and above, particularly those with additional cardiovascular risk factors. The results of this review support these guideline recommendations and underscore the need for continued emphasis on lipid management in diabetes care.

The strengths of this review include a focus on original studies, a mix of high-quality RCTs and real-world cohort data, and relevance to current clinical practice. However, certain limitations must be acknowledged. The exclusion of meta-analyses may have limited the ability to pool effect sizes. Additionally, some cohort studies may be subject to confounding or bias due to observational design. Despite these limitations, the findings offer a comprehensive and clinically relevant summary of statin therapy in the diabetic population.

CONCLUSION

Statins have been shown to significantly reduce the risk of cardiovascular (CV) events in individuals with diabetes. The evidence from both randomized controlled trials and observational studies supports their effectiveness in both primary and secondary prevention settings. High-risk diabetic patients, particularly those with established cardiovascular disease or multiple risk factors, derive the greatest benefit from intensive statin therapy. While concerns about statin-associated new-onset diabetes exist, particularly with high-intensity regimens, these glycemic effects are generally modest and outweighed by the cardiovascular benefits.

Given the strong and consistent evidence, statins should continue to be a central component of cardiovascular risk management in patients with diabetes. Early initiation, adherence, and individualized risk stratification should guide their clinical use to optimize outcomes.

Conflicts of interest: None Declared
Source of funding: None

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