

THE EFFICACY OF STATIN THERAPY IN REDUCING CARDIOVASCULAR ACCIDENT STROKE  
(CVA) RISK AMONG TYPE 2 DIABETES ADULT PATIENTS USING PATIENT-CENTERED CARE:  
AN INTEGRATIVE REVIEW

An Integrative Review

Submitted to the

Faculty of Liberty University

In partial fulfillment of

The requirements for the degree

Of Doctor of Nursing Practice

By

Simone Anckle

Liberty University

Lynchburg, VA

October 2023

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### **Abstract**

This study was an integrated review that comprehensively analyzed the efficacy of statin therapy in mitigating the risk of cardiovascular accidents (CVA) among individuals with type 2 diabetes mellitus (DM). The research seeks to explore statin management in preventing CVAs, a significant concern for this patient population. The study conducts a thorough synthesis of twenty-one peer-reviewed articles, critically evaluating the efficacy, safety, adherence factors, and cost-effectiveness of statin therapy for diabetic patients. The study adhered to the Whitmore and Knafelz Framework and used the constant comparison approach to systematically categorize and pattern findings, culminating in an integrated understanding of statin therapy's impact on CVA risk. The research results demonstrate a consistent and noteworthy reduction in CVA incidence among type 2 DM patients receiving statin therapy, showcasing a relative risk reduction of 30% in CVA incidence. The study stresses the efficacy of statin therapy in significantly reducing low-density lipoprotein cholesterol levels, a pivotal risk factor for cardiovascular diseases in DM patients. Safety evaluation revealed minimal adverse effects, emphasizing modern-intensity statins over high-intensity therapy and warning against use in patients with high 10-year CVD risk and rheumatoid arthritis patients who may suffer autoimmune complications. Furthermore, the project addresses critical aspects of clinical scholarship and analytical methodologies, employing rigorous analysis to synthesize existing literature. The findings advocate for statin therapy's integration into diabetes management guidelines, bridging the realms of scientific underpinnings, interprofessional collaboration, and advanced nursing practice. The findings have substantial implications for clinical practice and the overall well-being of the diabetic patient population, promoting evidence-based interventions and improved patient outcomes.

*Keywords:* Statin therapy, cardiovascular accidents (CVAs), Type 2 diabetes, efficacy, adherence, cost-effectiveness, patient-centered care, statin risk reduction, clinical outcomes

### **Dedication**

This research is dedicated to the countless patients and healthcare professionals whose resilience and dedication inspire us to continually strive for advancements in healthcare. It is a tribute to the individuals living with type 2 diabetes and to my best friend who died in Jan of 2023 at the age of 46 years with DM complications, whose courage in facing the challenges of this condition fuels my pursuit of knowledge and better treatments. Additionally, this work is dedicated to the memory of those who lost their lives to CVAs, reminding us of the urgency to seek effective preventive measures. Lastly, this research is dedicated to the pursuit of a healthier future for all, driven by the hope that our contributions will make a meaningful difference in the lives of many.



### **Acknowledgments**

I express my sincere gratitude to all individuals and organizations who contributed to the successful completion of this research. First and foremost, I extend my deepest appreciation to the Liberty University professors, mentors, and instructors, for their guidance and invaluable insights that formed the foundation of this study. Your willingness to share experiences and expertise has enriched the depth and quality of my integrative review.

To my preceptors, thanks for your trust and unwavering support throughout this integrative review endeavor and the constructive feedback that was instrumental in shaping the trajectory of this study and refining its methodology.

I extend my thanks and gratitude to my husband, son, both my parents, other families, and friends for their encouragement, patience, and understanding during this research journey. Your emotional support sustained me through the challenges and triumphs.

I appreciate my colleagues at the university for their continuous motivation and encouragement and it is an honor to reach this far with you all.

Lastly, I thank the academic community and the various research contributors whose work formed the basis of my review. Your pioneering efforts have paved the way for my understanding of statin therapy and its potential to reduce CVA risk among patients with type 2 diabetes.

**List of Abbreviations**

American College of Cardiology (ACC)

American Heart Association (AHA)

Atherosclerotic cardiovascular disease (ASCVD)

Cardiovascular diseases (CVD)

Cardiovascular accident (CVA)

Centers for Disease Control and Prevention (CDC)

Diabetes mellitus (DM)

Incremental cost-effectiveness ratio (ICER)

Low-density lipoprotein (LDL)

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

Quality-adjusted life-year (QALY)

Randomized control trial (RCT)

World Stroke Organization (WSO)

## **Section One: Introduction**

Cardiovascular diseases (CVDs) are the leading cause of morbidity and mortality worldwide, resulting in millions of deaths annually. Patients with diabetes mellitus (DM) are at higher risk of developing cardiovascular events, and the risk increases as the duration of diabetes and the presence of other comorbidities increase. Statins are commonly used for the primary and secondary prevention of CVDs, and recent clinical trials have demonstrated their effectiveness in reducing CVD events and mortality rates. However, there is still considerable debate about the optimal use of statins, especially in patients with DM. The purpose of this integrative review is to synthesize the available literature on the use of statins in adult patients with DM to reduce their risk for cardiovascular accident (CVA) since DM itself is a major risk factor of the condition. The review aims to provide a comprehensive understanding of the current evidence on the efficacy, safety, and cost-effectiveness of statin therapy in this adult population and the implications of its use on patient adherence and stakeholders. Ultimately, the review hopes to inform clinical practice and guide decision-making in the management of CVA risk in patients with DM.

### **Background**

Globally, CVA, or stroke, has become one of the most common cardiovascular events, with the World Stroke Organization (WSO) declaring that it has reached epidemic levels. The organization stated that one in four adults above 25 will experience a stroke in their lifetime, 12.2 million people will have their first stroke this year, and 6.5 million will die as a result (Feigin et al., 2022). Also, 60% of strokes occur in people under 70, and 16% occur in people under 50, meaning that stroke is not concentrated in the older adult category as would be thought, but in younger and more productive age groups (Feigin et al., 2022). The United States, like the rest of the world, has a large stroke burden. According to the Centers for Disease Control and Prevention

(CDC, n.d.), one in six U.S. deaths occurs due to stroke. Additionally, every 40 seconds a person in the US has a stroke, every 3.5 minutes a person dies from a stroke, and 610,000 new strokes occur every year, equating to \$53 billion in health care costs. DM is listed by the CDC as among the top four risk factors associated with stroke development, as individuals with type 2 diabetes have a two- to fourfold increased risk of developing cardiovascular events, including stroke (CDC, 2022). These findings create a great sense of urgency to develop stroke prevention measures among high-risk groups like diabetic patients.

Statin therapy has been shown to lower cholesterol levels and reduce the risk of cardiovascular events in high-risk patients. However, there is a lack of consensus regarding the optimal use of statins in DM patients. Some studies suggest that statins should be prescribed to all patients with type 2 diabetes regardless of their cholesterol levels, while others recommend statin therapy only for those with elevated cholesterol levels or those at high risk of CVD. Therefore, this integrative review appraises the current evidence regarding the effectiveness and safety of statin therapy in reducing the risk of CVA in patients with type 2 diabetes. The findings may have important implications for clinical practice, policymaking, and healthcare management related to the reduction of CVA and other cardiovascular events in patients with type 2 diabetes.

### **Defining Concepts and Variables**

An integrative review utilizes multiple studies to provide a comprehensive overview of a topic, and clear definitions of key terms ensure that analyzed studies are relevant and comparable (Toronto & Remington, 2020). As such, well-defined concepts and variables help readers understand the practical and clinical significance of the results.

### **Statin Therapy**

Statin therapy involves the administration of statin medications to manage and regulate cholesterol levels in individuals with type 2 diabetes (Armstrong & Little, 2019). Statins inhibit an enzyme in the liver that plays a crucial role in cholesterol synthesis, thereby reducing the overall level of cholesterol in the bloodstream. Statins have been shown to effectively lower cholesterol levels, particularly low-density lipoprotein (LDL) cholesterol (Kim et al., 2022). This reduction in cholesterol is crucial because elevated cholesterol levels are associated with an increased risk of CVDs, including strokes. Healthcare providers aim to mitigate cardiovascular risk and improve overall heart health in diabetic patients.

### **CVA Risk**

CVA risk describes the likelihood of an individual with type 2 diabetes experiencing a stroke (Tabesh et al., 2019). A stroke, or CVA, occurs when blood flow to the brain is altered, causing brain cell damage or death. Diabetic patients have a heightened risk of stroke due to various factors, including the effects of high blood sugar levels on blood vessels. Monitoring and addressing this risk is critical to prevent the occurrence of strokes, as strokes can severely impact an individual's health and quality of life.

### **Efficacy of Statin Therapy**

The efficacy of statin therapy refers to how well statin medications reduce the occurrence of cardiovascular events in individuals with type 2 diabetes (Kim et al., 2022). Researchers and healthcare professionals assess the efficacy of statin therapy by analyzing clinical trials and studies that investigate the impact of these medications on the risk of strokes. Assessing the efficacy of statin therapy requires ascertaining the statistical significance of the findings and the magnitude of the risk reduction observed in the patient population.

### **Adverse Events Associated With Statin Treatment Therapy**

Adverse events are unwanted, unexpected, or harmful effects experienced by individuals taking statin medications to manage cholesterol levels (Lee et al., 2023). While statins are generally well tolerated, some individuals may experience adverse effects, like muscle pain, liver abnormalities, or gastrointestinal discomfort. An understanding of the possible adverse events associated with statin therapy is important to clinicians' ability to perform a risk-benefit analysis regarding the appropriateness of statin use for each patient.

### **Cost-Effectiveness of Statin Therapy**

Assessing both the costs associated with statin treatment and the overall benefits in terms of improved health outcomes and potential cost savings for healthcare systems is critical (Armstrong & Little, 2019). This evaluation is essential for health organizations and physicians making informed healthcare resource allocation decisions. Cost-effectiveness analysis is crucial to determine whether the benefits of statin therapy in reducing CVA risk justify the associated costs.

### **Incremental Cost per Quality-Adjusted Life-Year (QALY) Gained**

The incremental cost per quality-adjusted life-year (QALY) gained is an essential economic measure used to assess the cost-effectiveness of various medical interventions (Amstrong & Little, 2019). This measure involves a comparison of the additional costs incurred due to an intervention with the additional QALYs gained as a result of the intervention. This measure aims to determine whether the benefits of improved health-related quality of life justify the additional costs. A lower incremental cost per QALY suggests that an intervention is more cost-effective.

### **Lipid Profile**

A lipid profile is a comprehensive measurement of different types of lipids, including cholesterol and triglycerides, present in the bloodstream (Fan et al., 2019). A lipid profile can be used to assess an individual's risk of developing CVDs such as strokes. The lipid profile includes measurements of high-density lipoprotein cholesterol, LDL cholesterol, total cholesterol, and triglyceride levels. Elevated levels of LDL cholesterol and triglycerides increase the risk of atherosclerosis and subsequent cardiovascular events (Fan et al., 2019).

### **Problem Statement**

CVA is a major health concern for patients with type 2 diabetes due to significant morbidity and mortality rates. While statin treatment has been shown to reduce the risk of CVA in this population, there is a continued lack of consensus regarding statin effectiveness and safety among this population, which has complicated efforts to effectively manage CVA risk in DM patients. A study by Panozzo et al. (2019) conducted over 10 years found that premature statin discontinuation was common among diabetic patients due to the perceived potential risk of worsening diabetes symptoms and other reasons, indicating a need for a more thorough assessment of statin use and efficacy. An integrative review of the current evidence to determine the efficacy of statin treatment in reducing CVA risk in these patients is warranted to assess statins' efficacy and cost efficiency, identify gaps in the literature for future research, and enhance decision-making regarding statin use to reduce CVA risk.

### **Purpose of the Integrative Review**

The purpose of this integrative review was to evaluate the effectiveness of statin treatment in reducing the risk of CVA among patients with DM. This integrative review aimed to synthesize and analyze the current literature on this topic to provide a comprehensive understanding of the effectiveness of statin treatment and to identify any gaps in the existing literature. The significance

of this review is in its potential to enhance clinical practice and improve patient outcomes by providing an understanding of the best interventions to prevent CVA in patients with type 2 diabetes.

### **Review Questions**

The clinical question for this review is, “Does the implementation of statin management among patients with type 2 diabetes improve outcomes and reduce the risk of CVA using a patient-centered approach to management?”

The following questions also guided the review process to further refine the clinical question:

1. What is the evidence regarding the effectiveness of statin therapy in reducing the risk of CVA among patients with type 2 diabetes?
2. What measures may work to enhance patient adherence to statin therapy in the context of type 2 diabetes?
3. What are the adverse events associated with statin therapy in patients with type 2 diabetes?
4. What is the cost-effectiveness of implementing statin therapy for reducing CVA risk in patients with type 2 diabetes?

### **Goals of the Integrative Review**

The review has several key goals within its purpose of comprehensively exploring the impact of statin therapy on patients with type 2 diabetes, particularly with reducing the risk of CVA. Firstly, it aims to systematically review and synthesize a body of peer-reviewed research articles. These articles serve as valuable pieces of evidence on the effectiveness of statin therapy as a preventive measure for CVA for patients with type 2 diabetes. Secondly, the review strongly



emphasizes the critical evaluation and analysis of the safety aspects associated with the use of statins in diabetes management. Ensuring the well-being of diabetic patients and minimizing potential risks of undergoing statin treatment is of utmost importance. Lastly, the review ventures into the realms of adherence and cost-effectiveness, seeking to shed light on the factors that influence patient compliance with statin therapy and the economic implications of such interventions. These multifaceted goals will aid the review in providing a holistic understanding of statin therapy's role in reducing CVA risk among individuals with type 2 diabetes, offering valuable insights for both clinical practice and health care policy.

## **Essentials of Doctoral Education for Advanced Practice Nursing**

### **Essential I: Scientific Underpinnings for Practice**

This integrative review is grounded in a scientific inquiry, aiming to assess the effectiveness of statin therapy in reducing CVA risk for patients with type 2 diabetes.

### **Essential II: Organizational and System for Quality Improvement and System Thinking**

This integrative review contributes to the broader perspective of enhancing quality in healthcare delivery. As such, it enhances the overall quality of health delivered on a broader scale, aligning with this essential. The Melnyk framework was rigorously applied to assess evidence quality and make assertions based on strong evidence support (Melnyk & Fineout-Overholt, 2015).

### **Essential III: Clinical Scholarship and Analytic Methods for Evidence-Based Practice**

The integrative review's central question required rigorous evaluation and synthesis of existing research to enhance evidence-based practices and holistically improve patient care.

### **Essential IV: Information System/Technology and Patient Care**

This integrative review leverages information systems and technology to access and analyze a wide array of research literature from databases.

### **Essential V: Health Care Policy for Advocacy in Health Care**

By focusing on the effectiveness of statin therapy in reducing CVA risk, the integrative review indirectly advocates for informed healthcare policies. The findings can contribute to policy discussions on the integration of statin therapy into diabetes management (AACN, 2006).

### **Essential VI: Interprofessional Collaboration for Improving Patient and Population Health Outcomes**

The integrative review encourages an interdisciplinary approach to ensure a holistic evaluation of statin therapy's impact on CVA risk, promoting improved patient and population health outcomes.

### **Essential VII: Clinical Prevention and Population Health**

The integrative review's focus on CVA prevention in patients with type 2 diabetes aligns perfectly with contributing to the improvement of population health on a broader scale.

### **Essential VIII: Advanced Nursing Practice**

This review epitomizes advanced nursing practice by evaluating the impact of a specific intervention, statin therapy, in a well-defined patient population, ultimately contributing to enhanced patient care.

### **Rationale for Conducting the Review**

This integrative review focuses on the efficacy of statin therapy in reducing CVA risk among type 2 diabetes patients using a patient-centered approach (Kim et al., 2022). CVD, including stroke, stands as a major cause of morbidity and mortality worldwide, and individuals with type 2 diabetes are particularly vulnerable to its devastating effects, with a two- to fourfold increased level of morbidity (CDC, n.d.). This review aims to address a pressing clinical need by examining the potential benefits of statin therapy, a widely used lipid-lowering intervention, in this high-risk population. Type 2 diabetes is consistently identified as a significant risk factor for cardiovascular events, and its coexistence with dyslipidemia further magnifies the risk. Given the rising prevalence of type 2 diabetes and the associated burden of cardiovascular complications, it is crucial to explore evidence-based interventions that can effectively mitigate the occurrence of CVA in this population (Singh et al., 2020). Statins are renowned for their ability to reduce LDL cholesterol and manage lipid profiles and have garnered attention as a potential intervention to reduce CVA risk in DM patients. By assessing the existing body of literature, this review aims to elucidate whether patient-centered statin therapy improves patient outcomes by reducing CVA risk.

Additionally, the economic implications of preventive interventions like statin therapy cannot be overlooked. Stressed healthcare systems create the need to assess not only the clinical efficacy of interventions but also their cost-effectiveness and potential ability to reduce healthcare costs. Evaluating the cost-effectiveness through measures like the incremental cost per QALY gained will inform policymakers and stakeholders of the economic feasibility of implementing statin therapy among the diabetic patient population (Armstrong & Little, 2019). The rationale for conducting this integrative review is underscored by the urgent need to address the escalating burden of CVA risk among type 2 diabetes patients. A synthesis of evidence from a range of studies

offers a comprehensive understanding of the potential benefits, safety, and cost-effectiveness of statin therapy.

### **Literature Review Breakdown**

The literature search for this study identified 21 articles from databases of peer-reviewed journal articles like PubMed, CINAHL, and Cochrane Library. The articles identified included 11 retrospective cohort studies, three systemic reviews, two randomized control trials (RCTs), one decision model analysis, one descriptive study, one case-control study, one prospective cohort study, and one quasi-experimental design. The review also explored data from the WSO, CDC, and American College of Cardiology (ACC) that provided crucial information like statistics and current practices related to the topic.

Among the various risk factors contributing to CVA, type 2 diabetes emerges as a prominent and modifiable determinant. Individuals with type 2 diabetes are predisposed to an increased risk of CVA, often leading to devastating outcomes (Kim et al., 2022). The prevalence of Type 2 diabetes continues to rise, creating an urgent need to develop effective interventions to curb CVA-related complications. Statin therapy holds promise as a strategy to mitigate CVA risk in patients with type 2 diabetes, as reducing LDL levels that are often significantly higher in diabetic patients, delays the progression of atherosclerosis and cardiovascular events in these patients, reducing CVA risk (Singh et al., 2020). However, the application of statin therapy warrants exploration. The evidence from clinical trials, observational studies, and other relevant sources shows the interplay between statin therapy and patient-centered care to optimize patient outcomes (Singh et al., 2020).

### **Supplemental Evidence**

In addition to the primary research articles discussed in the review, various supplemental sources further stress the importance of investigating the efficacy of statin therapy in reducing CVA risk among patients with type 2 diabetes (Toronto & Remington, 2020). The CDC provides comprehensive data and insights into the epidemiology of stroke, emphasizing its substantial impact on public health. The CDC's (n.d.) stroke facts highlight the prevalence, risk factors, and consequences of stroke, reinforcing the urgency of the implementation of preventive strategies to curb its incidence. Also, the WSO (2023) provides crucial information about stroke prevalence, etiologies, and complications. This source reinforces the urgency to act on stroke prevention.

## **Standards**

The 2018 ACC and American Heart Association (AHA) cholesterol management guidelines further strengthen the need for statin therapy among diabetic patients. These guidelines represent a significant advancement in the approach to managing blood cholesterol levels, including the use of statin therapy, particularly for diabetic patients. The guidelines were developed by a multidisciplinary panel of experts in CVD prevention, lipid management, and diabetes care to provide a comprehensive and evidence-based framework healthcare providers can use to make informed decisions about cholesterol management (Montovano et al., 2022). The risk-based approach advocated by the ACC/AHA guidelines reinforces the need to assess the risk-benefit ratio based on an individual's cardiovascular risk profile. The ACC/AHA guidelines stress shifting from a one-size-fits-all approach to a personalized, risk-based approach for cholesterol management (Montovano et al., 2022).

## **Review of Studies**

### **Efficacy and Incidence of Statin Use**

Panozzo et al. (2019) conducted a retrospective cohort study using Medicare claims data to assess the incidence of statin use in older adults with and without CVD and DM between January 2008 and March 2018. The study found that statin use increased in older adults with CVD and DM during the study period, but their prescription for patients with DM without CVD often lagged, despite DM patients having 2-4-fold risk of suffering a CVD than the general population (Panozzo et al., 2019). The study's strength was its use of a large and representative sample of older adults in the US. However, the study's retrospective design limited the establishment of a causal relationship between statin use and CVD risk reduction in patients with DM and precluded the ability to evaluate the effectiveness of statin therapy. Nonetheless, the study highlighted the underutilization of statins in older adults with DM, potentially leading to suboptimal CVA risk reduction.

McGurnaghan et al. (2019) examined the risk of cardiovascular events in patients with type 2 diabetes. The study's strengths were its retrospective design and large sample size, which increases reliability, but its weakness was in its use of a broad definition of CVD that may not reveal the severity and treatment of the elevated risk factors. Still, the study provides useful evidence showing that CVD risk is significant in DM patients, and these patients often have unmet needs and require intensive clinical interventions like statin therapy to prevent cardiovascular events. The study encourages tailored approaches to reduce the CVD burden that is significantly higher in DM patients.

Fan et al. (2019) conducted a cross-sectional study using National Health and Nutrition Examination Survey data from 2007 to 2014 to assess the association of residual hypertriglyceridemia and estimated atherosclerotic CVD (ASCVD) risk for U.S. adult diabetic patients using statins. The study found that residual hypertriglyceridemia was associated with a

higher ASCVD risk. Statin use reduced this risk, but residual hypertriglyceridemia persisted in patients with diabetes, regardless of statin use. The study's strengths were its large sample size and use of nationally representative data. However, the study's cross-sectional design limits the establishment of a causal relationship between statin use and ASCVD risk reduction in patients with diabetes. Still, the study adjusted for multiple confounding variables, including age, sex, ethnicity, body mass index, smoking status, and blood pressure, which increased internal validity and made the findings, which support statin use to reduce CVA risk, more dependable, as ASCVD is a risk factor for CVA.

Jung (2021) conducted a retrospective cohort study to investigate the association between statin use and CVD outcome risks among individuals with varying predicted CVD risks in Korea. The study found that statin use was associated with a reduced risk of adverse CVD-related outcomes and all-cause mortality, and the benefit was greater in patients with a higher predicted CVD risk. The study's strengths were its use of a large cohort of patients with different predicted CVD risks and the availability of abundant national insurance data. The study's retrospective design limited the establishment of a causal relationship between statin use and CVD risk reduction in patients with type 2 diabetes, as it was an observational study. Still, the study provided interesting findings that statin uses significantly reduced the risk of major cardiac events and all-cause mortality in those with a predicted 10-year CVD risk of  $\geq 10\%$  but an increased risk of all-cause mortality for those with a 10-year CVD risk of  $< 10\%$ . These findings support the current guidelines recommending statin therapy for patients with an estimated 10-year CVD risk of  $> 7.5\%$  (Montovano et al., 2022).

Singh et al. (2020) conducted a systematic review and meta-analysis to evaluate the role of statins in the primary prevention of ASCVD and mortality in patients with mean cholesterol in the

near-optimal to borderline high range. The study found that statin therapy was associated with a reduced risk of major adverse cardiovascular events, including stroke, in patients with borderline high cholesterol levels. The strengths of this study lay in the systemic review of RCTs, which represents Level I evidence, and its limitations emerged from the different designs and baseline characteristics of studies used. Still, the study strongly supports the use of statins in patients with type 2 diabetes to reduce the risk of CVA.

Bailey and Marx (2019) conducted a literature review of clinical trials on statin cardiovascular protection in type 2 diabetes. The article highlights the results of several large-scale clinical trials that have demonstrated the efficacy of statin therapy in reducing the risk of cardiovascular events in patients with type 2 diabetes. Bailey and Marx discussed how newer glucose-lowering medications, such as sodium-glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists, have shown significant cardiovascular benefits beyond their glucose-lowering effects. The authors recommended that statin therapy be initiated in all patients with type 2 diabetes to reduce the risk of cardiovascular events. The strength of this article was that it provides a comprehensive review of the available clinical trial evidence on the use of statins in patients with type 2 diabetes, and the limitations lay in the reliance on studies in which participant characteristics, sample size, and duration varied. Still, the study provided conclusive findings that statins have a significant positive impact on CVA risk.

### **Safety of Statin Therapy**

Kim et al. (2022) investigated the relative contributions of statin intensity, achieved LDL cholesterol level, and statin therapy duration to CVD risk reduction in patients with type 2 diabetes. The study had a large sample size of 43,409 patients, and the authors used a population-based cohort design to investigate the research question. The results proved that statin intensity and LDL



cholesterol level significantly reduced CVD risk in patients with type 2 diabetes. Despite the study's design being observational, the findings provided crucial insights that address the clinical question.

Lee et al. (2023) investigated the effectiveness of moderate-intensity statin therapy with ezetimibe compared to a high-intensity statin in patients with diabetes and ASCVD disease. The study's strengths lay in it being an RCT that offers credible findings that the two treatment strategies were equally effective in reducing cardiovascular events, though high-intensity statin therapy had a higher complication possibility rate than moderate statins in diabetic patients with ASCVD. Still, the sample population was relatively small, and the follow-up period was short.

Jun et al. (2021) investigated the use of statins for CVD primary prevention in patients with type 2 diabetes and whether the therapy can benefit all ages. The study's strengths were in the large sample size of 268,018 patients and its nationwide propensity-matched cohort design, while its weaknesses were lack of generalizability due to being a one-nation study done only in Korea. Still, the results showed that statin use was associated with a lower incidence of CVD events in patients with type 2 diabetes, regardless of age.

Wierzbicki (2018) evaluated various lipid-lowering interventions, particularly focusing on LDL-cholesterol and other related factors, in the management of the possible cardiovascular risks associated with DM. The study has strengths in that it is a systemic review of clinical trials, which means the results offer high-quality evidence. However, the reliance on existing literature means that any potential weaknesses of those studies may affect reliability, and selection bias may also have occurred due to poor sampling procedures for articles used in the study. Still, the study

supports the use of statins in LDL-cholesterol management, which would translate to reducing CVA risk, as LDL is associated with an increased risk of cardiovascular events.

Tabesh et al. (2019) investigated the use of statins across the globe to gain deeper insight into the extent of their use and their effectiveness in managing cardiovascular risks in type 2 DM patients. The strengths of this study lie in its retrospective design and large sample from many countries, which increases generalizability. The study's weaknesses could be the failure to focus on this review's clinical question directly. However, it offers significant support for statin therapy as an effective intervention for cholesterol management in type 2 DM patients with minimal risks. As such, lipid-lowering drugs may be useful in lowering CVA risk through managing risk factors like high cholesterol.

Ozen et al. (2023) conducted a cohort study to evaluate the reduction of CVD and mortality risk for patients with rheumatoid arthritis (RA) taking statins and the risk of new-onset DM in those patients. The study found that statin use was associated with a reduced risk of CVD and mortality but an increased risk of new-onset DM in patients with RA, creating new considerations for practitioners managing statin use in patients with RA. The study's strength is its use of a large cohort of patients with RA, although the study's limited focus on RA patients makes findings hard to generalize to all patients with type 2 diabetes. Still, the study offered significant insights into the possible impact of statin use in DM patients with RA.

Malmberg et al. (2021) investigated compliance with primary prevention statin therapy and its association with CVD risk and death in low-risk patients with type 2 diabetes. The study's strengths were a larger sample size of 2,081 patients and the prospective cohort design. Despite

having the limitation of relying on prospective data, the researchers concluded that statin therapy lowered the incidence of cardiovascular events and death.

Rana et al. (2018) investigated the risk of incident ASCVD disease events by achieving atherogenic lipid levels among 62,428 statin-treated individuals with DM. The strengths of this study lie in the large sample size, although failure to focus on aspects investigated by this review's clinical question is a significant limitation. The results showed that lower achieved LDL cholesterol and non-high-density lipoprotein cholesterol levels were associated with a lower incidence of CVD events. The findings, when viewed in conjunction with those from other studies, provided meaningful evidence.

Kuo et al. (2021) conducted a nationwide case-control study to evaluate the impact of statin therapy on long-term outcomes in patients with end-stage renal disease and acute myocardial infarction. They found that statin therapy reduced the risk of mortality in these patients. The strengths of this study lie in the use of a nationwide sample that increased representativeness and the study's investigation of impacts from a long-term perspective. However, the study does not directly address this review's clinical question of whether the implementation of statin therapy in patients with type 2 diabetes reduces the risk of CVA. Still, since end-stage renal disease is a common comorbid condition in diabetic patients, interpreting the findings in conjunction with those from other studies significantly supports the clinical question.

Ferrières et al. (2018) conducted a cross-sectional study to evaluate the achievement of lipid-lowering therapy goals in high-risk patients from French general practice. The authors found that a significant proportion of high-risk patients (52.8%) did not achieve their lipid-lowering therapy goals. The strengths of the study were the use of a large and diverse sample population

and a rigorous methodology used to define and measure lipid-lowering therapy, while the limitations lay in the study's failure to directly assess the efficacy and safety of statin therapy in patients with type 2 diabetes or to account for other lifestyle interventions. Ferrières et al. (2018) suggested that achieving lipid-lowering therapy goals is crucial in high-risk patients, and statin therapy is a commonly used lipid-lowering therapy. The study highlighted the importance of setting and achieving lipid-lowering therapy goals in high-risk patients, like type 2 diabetes patients. Therefore, interpreting these findings with those from other studies offered valuable insights that support the clinical question.

Lan et al. (2019) investigated the effectiveness of decision-support algorithm systems in the control of glucose in people with type 2 DM and cardiovascular problems. The strengths of the study lay in the observational design that made it easy to collect data from the natural setting while the systems were in operation, while the possible weaknesses were the single-centered design and the short period during which the study was conducted. However, the study provided dependable findings that decision support systems may recommend statin prescription and lead to an average 10mm/l reduction in blood glucose levels, which would significantly reduce CVA risk. As such, while statin prescriptions are generally uncommon, using decision support systems could increase the use of these prescriptions, leading to better patient outcomes.

### **Cost-Effectiveness**

Armstrong and Little (2019) analyzed the cost-effectiveness of interventions to improve adherence to statin therapy in patients with ASCVD in the US. They used a decision model to evaluate the costs and benefits of educational programs, behavioral counseling, and mobile health technologies. The researchers found that interventions improved adherence to statin therapy and were cost-effective in reducing the risk of cardiovascular events in patients with ASCVD. The

strengths of the study lay in the decision analytics model used to estimate the cost-effectiveness of interventions and the assessment of different interventions, including nurse-led and electronic. Still, the study relied on hypothetical participants, did not directly assess the efficacy and safety of statin therapy in patients with type 2 diabetes, and did not provide clinical effectiveness. The article still found that interventions that encourage statin adherence are cost-effective and significantly reduce the risk of cardiovascular events in high-risk patients.

### **Adherence and Compliance Factors**

Kamal et al. (2018) aimed to assess the effectiveness of a talking prescription intervention to improve adherence to statin therapy among stroke and heart attack survivors. The study used an RCT design and assigned participants to the talking prescription intervention or usual care. The study's strengths include the randomized design and objective adherence measures. However, the study was limited by potential selection bias and a short 3-month intervention period. Still, it offered Level II evidence and implications for stakeholders on the need to encourage statin adherence to reduce CVA risk.

Mohan et al. (2021) investigated the impact of motivational interviewing on adherence to medication in patients with diabetes and high risk of CVD. The study's strengths lay in the use of a cohort design with an experimental and control group, while its weaknesses were its small sample that may have suppressed the differences between the groups. Still, the study emphasized the need for effective nonpharmacological measures to enhance adherence as a measure to reduce complications and health care costs.

Hisni et al. (2019) investigated the impact of a cardiovascular self-management support program on the prevention of cardiovascular complication behaviors and clinical outcomes among

DM patients. The strengths of the study lay in its quasi-experimental design, which provides relatively good quality evidence, while its weaknesses were in the lack of a control group, which often makes generalization difficult. However, significant improvements in cardiovascular complication behaviors and clinical outcomes after program implementation suggest that such a program may be effective in this population. The article’s findings, interpreted alongside those from other studies, may offer dependable evidence that consistent statin therapy reduces CVA risk, as taking statins is not enough without a consistent self-program that encourages adherence and health behaviors. These articles stress the importance of statin adherence and other nonpharmacological management strategies as an approach to achieve CVA risk reduction as strict adherence to medication and self-management directly impact the efficacy.

**Inclusion and Exclusion Criteria**

The literature search focused on studies that included at least one major keyword like *statin management, type 2 diabetes, CVA, stroke, interventions, CVDs, cardiovascular events, and outcomes*. The search was limited to studies published in the English language within the past 5 years (2018-2023). Also, articles had to be fully accessible, and peer-reviewed to be included in the literature review. After the inclusion criteria were applied, 21 studies were selected for inclusion in the review. Included in the review were RCTs, cohort studies, decision analysis models, and systematic reviews.

**Table 1**

*Inclusion and Exclusion Criteria*

Criterion	Included	Excluded
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Published Date	2018–2023	Before 2018
Keywords	Included keywords like statin management, type 2 diabetes, stroke, CVA, CVD, cardiovascular events, adherence	Did not include keywords like statin management, type 2 diabetes, stroke, CVA, CVD, cardiovascular events, TIA
Peer review	Peer-reviewed articles and guidelines	Non-peer reviewed articles
Publication language	English	Non-English
Availability	Article with accessible full text	Non-full articles

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**Conceptual Framework**

The Whitmore and Knafl (2005) and the Toronto and Remington (2020) frameworks provided rigorous guidance that aided the construction and development of this integrative review.

**Whitmore and Knafl**

Whittemore and Knafl (2005) proposed a systematic approach to synthesizing existing research studies and offered a step-by-step framework for conducting an integrative review. The model consists of five main phases: (1) problem identification and planning, (2) literature search, (3) data evaluation, (4) data analysis, and (5) presentation of results. The use of the model is crucial for the review’s goal of providing a holistic understanding of statin therapy from safety, adherence, and efficacy perspectives to be achieved (Toronto & Remington, 2020).

***Problem Identification and Planning Phase***

The first phase involved identifying the problem and planning the study, which included defining the research question, establishing the scope and objectives, and identifying the stakeholders and resources needed for the study (Whittemore & Knafl, 2005). The question developed from the current inconclusive position of the effectiveness and safety of statins among DM patients was, “Does the implementation of statin management among patients with type 2 diabetes improve outcomes and reduce the risk of CVA using a patient-centered approach to management?” The formation of a clear clinical question allowed review questions to be defined to further answer the question from a holistic view.

### ***Literature Search Stage***

The second phase involves a comprehensive search of relevant literature. Multiple databases and sources were utilized for the literature search to ensure a thorough exploration of the topic. The search strategy was transparent, replicable, and based on a search strategy and inclusion and exclusion criteria (Whittemore & Knafl, 2005). Relevant articles were obtained by reading the abstracts and evaluating their relevance using the Critical Appraisal Skills Program tool before the article was included for evaluation.

### ***Data Evaluation Stage***

In the third phase, an assessment of the quality and relevance of the included studies occurred. This evaluation process involved assessing the study design, sample size, data collection methods, and other relevant factors to ensure the articles were suitable for the study. This step is crucial, as the reliability of any integrative review relies on the reviewer’s ability to systematically identify and analyze evidence-based sources (Toronto & Remington, 2020).



The validity and reliability of the chosen studies are critical to the ability to develop dependable evidence-based conclusions. For this reason, the Critical Appraisal Skills Program tool was used to assess the validity and reliability of the included studies. The Critical Appraisal Skills Program tool is a set of standardized critical appraisal checklists that evaluate the quality of research studies. It helps reviewers assess an article's validity, reliability, and relevance to a specific clinical question. In this critical appraisal, the Critical Appraisal Skills Program tool was used to evaluate the following aspects of each of the 21 studies: study design, appropriateness of the design for the research question, recruitment strategy, data collection, and analysis. The studies had a moderate to high level of validity and reliability, suggesting that they were well-designed and implemented and that the findings could be trustworthy. Also, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist served as a comprehensive guide for the systematic and transparent reporting of the review process. The checklist enables adherence to best practices in the conducting and reporting of systematic reviews. The checklist covers key aspects of the review, including the formulation of research questions, development of a search strategy, study selection, data extraction, and presentation of results to ensure the sources are qualified to answer the clinical question. Melnyk's Levels of Evidence framework by Melnyk and Fineout-Overholt (2015) provided a structured approach for assessing the strength of evidence generated by individual studies. The Melnyk framework was instrumental in the critical appraisal of the methodological quality of each included study and the determination of the overall strength of evidence in a range of Level I–VII, with Level I being the strongest.

### ***Data Analysis Stage***

The fourth phase was data analysis, where the extraction of relevant data from each study and the organization of the data in a meaningful way occurred (Toronto & Remington, 2020). An

evidence matrix was created to present key findings, concepts, theories, and other relevant information in tabular format. The author identified patterns, themes, and relationships across the studies to develop primary themes related to the topic.

**Constant Comparison Method.** The fourth phase begins with comparing and contrasting findings from individual studies (Whittemore & Knafl, 2005). Identification of recurring patterns, themes, and variations across studies helped develop meaningful themes and draw conclusions based on a comprehensive overview of the evidence from a holistic perspective.

**Data Reduction.** Data reduction was pivotal in managing the voluminous information gathered from diverse studies (Whittemore & Knafl, 2005). The phase involved condensing and summarizing data and extracting useful information related to study characteristics, interventions, outcomes, and results. Condensing the data helped the researcher to distill the core findings while maintaining the integrity and richness of the evidence.

**Data Display.** The phase focused on visually organizing the summarized data to facilitate a coherent representation of key concepts and themes. An evidence matrix was constructed to systematically present the characteristics of each study along with relevant findings related to measurable outcomes (Whittemore & Knafl, 2005). The evidence matrix offered a structured platform through which the various studies' contributions to the research question could be exhaustively compared and contrasted.

**Data Comparison.** The data comparison phase analyzed and juxtaposed the findings across studies to identify commonalities, discrepancies, and trends (Whittemore & Knafl, 2005). Themes related to the reduction in CVA risk, adherence to statin therapy, adverse events, and cost-effectiveness were synthesized to derive holistic insights into the implications of statin therapy for

diabetic patients. This comparison process enabled the development of a comprehensive narrative that addressed the research question.

**Conclusion Drawing and Verification Drawing.** The final phase entailed synthesizing evidence to answer the research question. The integration of the findings from diverse studies generated evidence-based conclusions regarding the effectiveness of statin therapy in reducing CVA risk among patients with type 2 diabetes (Whittemore & Knafl, 2005). These conclusions emerged from a rigorous process of cross-referencing and validation, which ensured that the conclusions were grounded in the collective evidence presented in the review. This methodology ensured that the synthesis of evidence was comprehensive, reliable, and able to contribute to the understanding of statin therapy and CVA risk reduction for diabetic patients.

### ***Presentation of Results***

The fifth phase of the model is the presentation of results. The final phase involves advocacy for policy changes or interventions that would improve statin therapy use among patients with type 2 diabetes based on the evidence generated by the study (Whittemore & Knafl, 2005). Based on the evidence in the review, the proposed intervention could reduce CVA risk in DM patients while applying caution in patients with a 10-year CVD risk < 10% and those with RA, who were shown to have adverse outcomes, especially the risk of worsening auto-immune problems. This stage was facilitated by an evidence matrix, a figure, and a PowerPoint for integrative review defense. Evaluation measures like the proportion of DM patients prescribed statins, medication adherence rates, and the incidence of CVA in these patients were established as success markers.

### **Toronto and Remington**

Toronto and Remington's (2020) guidance for integrative reviews significantly informed the development of this paper. Their methodology provided a structured approach that guided the synthesis of a diverse range of research findings. They encourage clearly defining the research objectives and the scope of the integrative review, ensuring the study has a focused and purposeful direction. Toronto and Remington stressed the importance of a comprehensive search strategy, and this advice ensured a broad spectrum of research relevant to the topic was included. Their framework also emphasized the need for a systematic approach to data analysis and the constant comparison method is also recommended by Toronto and Remington to categorize and synthesize the data effectively. Toronto and Remington's (2020) guidance served as a cornerstone for the development of this paper, providing a systematic and structured approach that helped navigate the intricacies of an integrative review.

## **Section Two: Comprehensive and Systematic Search**

### **Search Organization and Reporting Strategies**

The organization and reporting strategies employed in this integrative review adhere to the framework proposed by Whitemore and Knafl (2005), who advocated a systematic and comprehensive approach to synthesizing existing research. This approach ensures transparency, rigor, and replicability in the review process. The approach ensures that the review process is exhaustive enough to provide reliable evidence as the demand for quality evidence-based recommendations has increased considerably as value-based care increases (Toronto & Remington, 2020). The credibility and applicability of the findings are critical, as they inform clinical practice and policy decisions.

### **Search Strategy**

The following search strategy was used to identify relevant studies for the integrative review. A comprehensive search of electronic databases including PubMed, CINAHL, and Cochrane Library was conducted. The keywords used were *statin management, type 2 diabetes, CVA, stroke, interventions, CVDs, cardiovascular events, and outcomes*. The search was limited to studies published in the English language within the past 5 years (2018–2023). A total of 300 studies were initially identified. The articles included in the study are those whose titles and abstracts showed that they investigated the effectiveness of statin management among patients with type 2 diabetes in reducing the risk of CVA, those exploring the incidence of statin use, and cost-effectiveness and of adherence to statin use. Also, articles had to be fully accessible, and peer-reviewed to be acceptable for literature review. After applying the inclusion criteria, 21 studies were included in the review. RCTs, cohort studies, decision analysis models, and systematic reviews were included in the review. A table of evidence was used to analyze the literature (see Appendix A).

**Melnyk Pyramid.** The use of a hierarchical framework that categorizes different types of evidence based on their level of quality and relevance to clinical decision-making is crucial. The framework provided a structured approach to evaluating the strength of evidence (Melnyk & Fineout-Overholt, 2015). In the context of the current study, the Melnyk Pyramid of Evidence guided the search, selection, and assessment of relevant literature. The pyramid helped the investigator to identify the types of evidence that were most relevant to the research question. By referring to the pyramid, the investigator was able to prioritize systematic reviews, meta-analyses, RCTs, and retrospective cohort studies as the highest quality evidence. This approach enhanced the validity and reliability of the study's conclusions and recommendations for clinical practice and policy.

**PRISMA Statement.** The PRISMA model significantly enhances the quality and transparency of the integrative review. Its structured framework enhances various aspects of the study, leading to a more rigorous and reliable review process. The PRISMA model sets clear guidelines for reporting various aspects of the review process, including study selection, data extraction, and results synthesis (Page et al., 2021). The flow diagram ensures that every step of the review is transparently documented. This transparency enhances the credibility and replicability of the review, as readers can easily follow the systematic process used to select, evaluate, and synthesize evidence (Moher et al., 2009). A PRISMA flowchart can be found in Appendix C.

### **Terminology**

The integrative review entailed a strategic and comprehensive search strategy that incorporated specific terminology and Boolean operators. The terminology played a crucial role in the identification of relevant articles and in refining the search process. The terms of focus were *statin therapy*, *diabetes*, *CVA risk*, *adherence*, *stroke risk*, *cardiovascular events*, *cost-effectiveness*, and *efficacy*. These words ensured that articles specifically related to the topic were obtained. Also, the use of operators like *and or* were critical in the search process. The approach facilitated the identification of relevant articles that contributed to a comprehensive understanding of the efficacy of statin therapy in reducing CVA risk among type 2 diabetes patients.

### **Limitations**

Several limitations influenced the review process and the findings. These limitations should be acknowledged to ensure a balanced interpretation of the results (Toronto & Remington, 2020). In the case of a single individual conducting the review, there is a potential for bias and subjectivity in the selection of studies, data extraction, and interpretation of findings. Collaborative

efforts and peer input could have reduced potential bias. Also, statin therapy and diabetes management are evolving, and new studies may have been published after the review was conducted. The inclusion of studies published only until a certain point may limit the review's currency. Variability in designs, populations, interventions, and outcome measures across selected studies may have hindered direct comparisons and generalizability of findings or influenced the cohesion of the synthesized evidence.

### **Section Three: Methodology**

#### **Design**

This integrative review utilized a qualitative approach to synthesize and analyze existing research. A qualitative approach was chosen to enable a comprehensive understanding of the multifaceted aspects of this topic, allowing for in-depth exploration of the research findings. The literature selection process involved a systematic search across various scholarly databases, adhering to predefined inclusion and exclusion criteria and aligning to the PRISMA and Melnyk Pyramid. The search strategy was devised to identify relevant articles related to statin therapy and its impact on CVA risk in type 2 diabetes patients. After the initial search, a total of 21 articles were identified that met the inclusion and exclusion criteria, forming the basis of this integrative review. The review adopted the Whitemore and Knafl (2005) framework, providing a structured methodology for data analysis and synthesis. This framework encompasses strategies such as reduction, display, comparison, integration, and interpretation. It facilitated the organization of data, comparison of findings, and integration of themes that emerged from the research, enhancing the rigor and coherence of the analysis. Data extraction and theme development focused on key findings, methodologies, and outcomes, and the emerging themes were then presented and synthesized to provide a comprehensive understanding of the topic. The data were presented in a

clear and structured manner, adhering to the themes that emerged from the research, ensuring a logical flow and effective communication of the findings.

### **Measurable Outcomes**

The measurable outcomes were as follows:

- Efficacy of statin therapy in reducing CVA risk in DM patients.
- Safety of statin therapy – the risk-benefit ratio of their use.
- Cost-effectiveness of statin management.
- Improved patient adherence to statin therapy.

The measurable outcomes are of critical relevance to this study. Each of these outcomes is intricately linked to the central investigation concerning the impact of statin therapy on reducing the risk of CVA in patients diagnosed with type 2 diabetes. The efficacy of statin therapy directly addresses the fundamental question of whether these medications effectively contribute to reducing the risk of CVA, a vital concern for individuals with diabetes. Assessing the safety of statin therapy in terms of a risk-benefit ratio is essential for making informed clinical decisions and ensuring patient well-being during treatment. Moreover, evaluating the cost-effectiveness of statin management is pivotal in understanding the economic implications of implementing this therapy and its potential broader societal benefits. Lastly, improved patient adherence to statin therapy is crucial for ensuring the efficacy of treatment and, consequently, the reduction in CVA risk. Collectively, these measurable outcomes provide a comprehensive understanding of the effectiveness, safety, economic implications, and patient-centered aspects of statin therapy, enhancing the robustness and applicability of the study's findings.

### **Ethical Consideration**



The ethical considerations for this integrative review were meticulously addressed to ensure integrity. Before commencing the integrative review, a comprehensive application outlining the integrative review methodology, data collection, and potential ethical considerations was submitted to Liberty University's Institutional Review Board (IRB) for approval. Approval was granted, affirming that the integrative review design and protocols met the required ethical standards. Additionally, to further bolster the ethical foundation of the integrative review, the reviewer completed the Collaborative Institutional Training Initiative (CITI) training. This training provided a comprehensive understanding of research ethics, emphasizing the importance of respecting the rights and welfare of research participants, data handling, and confidentiality. A copy of the CITI certificate is attached in Appendix F.

### **Data Collection**

The data collection for this integrative review involved a systematic and comprehensive approach to ensure a thorough exploration of relevant literature (Whitmore & Knafl, 2005). The following methods were employed to gather data from diverse and reputable sources. The researchers utilized multiple databases to obtain a broad spectrum of literature. The selected databases included CINAHL, Promax, PubMed, and Cochrane. These databases were chosen for their extensive coverage of health-related research articles and their relevance to the study's focus. A comprehensive search strategy was designed to identify relevant articles related to the study's primary focus. The search strategy incorporated specific keywords such as "statin management," "type 2 diabetes," and "CVA" to ensure a targeted approach. The search employed appropriate medical terminologies and Boolean operators (e.g., AND, NOT) to refine the search and enhance its specificity. Boolean terms were used to combine keywords effectively, ensuring the inclusion

of relevant articles while excluding irrelevant ones. Articles were selected based on predefined inclusion criteria and articles meeting these criteria were included in the data collection process.

### **PRISMA Flow Diagram**

The search initially produced a total of 300 articles from electronic databases, including PubMed, CINAHL, and the Cochrane Library. The titles and abstracts of the 300 articles were screened against the inclusion and exclusion criteria, and 130 articles were deemed potentially relevant. The full texts of the 130 potentially relevant articles were retrieved and assessed for eligibility using the specified criteria. After the full-text review, 21 articles were determined to meet the criteria for inclusion in the integrative review. During the screening and full-text review phases, articles irrelevant to the research question or intervention ( $n = 82$ ), lacking focus on statin therapy and CVA risk in type 2 diabetes patients ( $n = 63$ ), or inappropriate in study design or methodology ( $n = 23$ ), as well as duplicate articles ( $n = 4$ ), were excluded. The integrative review ultimately included 21 articles that met the eligibility criteria for the current study. A flow diagram of the literature selection process can be found in Appendix C.

The comprehensive and systematic search of literature produced 21 articles that helped answer the clinical question and the review questions. The review included 11 retrospective cohort studies (Jun et al., 2021; Jung, 2021; Kim et al., 2022; Lan et al., 2019, Malmborg et al., 2021; McGurnaghan, et al., 2019, Mohan et al., 2021; Ozen et al., 2023; Panozzo et al., 2019; Rana et al., 2018; Tabesh et al., 2019), three systemic reviews (Bailey & Marx, 2019; Singh et al., 2020; Wierzbicki, 2018), and two RCTs (Kamal et al., 2018; Lee et al., 2023). The review also included one decision model analysis (Armstrong & Little, 2019), one descriptive study (Ferrières et al., 2018), one case-control study (Kuo et al., 2021), one prospective cohort study (Fan et al. 2019), and one quasi-experimental study (Hisni et al., 2019). These studies aligned with the topic of focus

and problem statement and helped answer the clinical question. These articles presented evidence on statin therapy efficacy, safety, and cost-effectiveness, as well as factors associated with adherence.

### **Timeline**

A table showing the timeline of different project activities is attached in Appendix E.

### **Feasibility of Analysis**

The feasibility of analysis for this integrative review was carefully considered to ensure that the study objectives could be effectively met. Given the scope and nature of the integrative review, a multifaceted approach was adopted to analyze the diverse data collected from various sources. The feasibility of this analysis was supported by a structured approach to data extraction, allowing for consistent and organized retrieval of information from the selected articles. This structured format facilitated the subsequent analysis by categorizing and presenting the data clearly and systematically. The Whitemore and Knafl (2005) framework provided a robust structure for data analysis through the well-defined reduction, display, comparison, integration, and interpretation strategies that ensured coherent and relevant synthesis of the diverse findings. Thematic analysis was chosen as a feasible method to identify and extract relevant themes from the literature. This allowed for the organization of data into meaningful patterns and concepts, enabling a deeper understanding of the efficacy, safety, cost-effectiveness, and adherence factors associated with statin therapy.

## **Section Four: Quality Appraisal**

The quality appraisal process serves as a critical component of rigorous evidence synthesis, as it allows for the assessment of the methodological robustness and reliability of included studies

in the integrative review. Ensuring the credibility and validity of the findings is essential to inform evidence-based decision-making (Toronto & Remington, 2020). By engaging in a meticulous quality appraisal process, the investigator aimed to enhance the overall trustworthiness of the synthesized evidence, further supporting the formulation of well-informed conclusions and recommendations for practice and policy.

This integrative review proposal was approved by the Liberty University Institutional Review Board, which ensured that the integrative review adheres to ethical guidelines. Although this study did not involve human participants, the investigator completed Collaborative Institutional Training Initiative certification on the ethical considerations required for high-quality research. The training module emphasized proper citation and acknowledgment of original authors to ensure academic integrity and ethical practice. The certificate obtained reflects the researcher's knowledge and understanding of research ethics, integrity, accuracy, transparency, critical appraisal, data extraction, synthesis, and reporting and writing skills. This training equipped the researcher with the necessary ethical foundation to conduct the literature review with integrity and professionalism. Adherence to ethical principles of reporting and writing is crucial in disseminating research findings and accurately representing the literature without plagiarism and falsifications. The Collaborative Institutional Training Initiative certificate can be found in Appendix F.

### **Sources of Bias**

During the quality appraisal process, potential sources of bias within the selected studies were systematically evaluated to assess their impact on the validity and reliability of the findings. Bias could have arisen from various factors such as study design, participant selection, data collection methods, and data analysis techniques (Toronto & Remington, 2020). The assessment

aimed to identify any sources of bias that might have influenced the results and conclusions of the individual studies, thus allowing for a more nuanced understanding of the limitations and implications of the evidence synthesized in this review. The study relied on secondary literature, and any weaknesses within those sources could have affected the quality of this review.

### **Internal Validity**

The believability of findings is crucial when conducting an integrative review to establish evidence-based literature (Toronto & Remington, 2020). Determining the extent to which the research designs and methodologies employed support causal inferences is critical. Internal validity encompasses aspects like randomization, blinding, control of confounding variables, and the overall rigor of the study design. This review ensured that all articles selected addressed the clinical question in one way or another and so conclusions could be drawn in response to the review questions. Also, studies not directly addressing the clinical questions were interpreted with other studies for a more comprehensive understanding.

### **Appraisal Tools**

To systematically evaluate the methodological quality of each included study, the investigator developed a literature matrix based on the Melnyk Pyramid. The matrix facilitated the assessment of key methodological components such as research objectives, sample characteristics, data collection methods, statistical analysis, and potential biases. Since the matrix presents the appraisal results in a structured manner, it allows for easy comparison and identification of strengths and limitations across the studies. Appendices A and B contain the literature matrix and the Melnyk Pyramid of evidence.

### **Reporting Guidelines**

The reporting guidelines proposed by Whitemore and Knafl (2005) were used to structure the quality appraisal process. These guidelines describe a systematic approach that ensures that each step of the appraisal process is rigorously conducted, consistent, and transparent. The guidelines were used by the investigator to evaluate the studies' methodological strengths and limitations, enhancing the overall credibility of the synthesized evidence. Adherence to the reporting guidelines helped the investigator maintain a rigorous and systematic approach in assessing the quality of the included studies and subsequently concluding the evidence synthesis.

### **Applicability of Results**

The investigator further contextualized the synthesis of findings from the selected studies by considering the applicability of the results within the identified themes. As different studies addressed various aspects of statin therapy, such as effectiveness, safety, adherence, and cost-effectiveness, assessing the applicability of these findings to the patient-centered approach emphasized in this review was crucial. The identified themes provided a framework for consideration of how the synthesized evidence aligns with the objectives of the study and its ability to inform practice and policy recommendations (Whitemore & Knafl, 2005). The findings derived from this study hold significant relevance for both clinical practice and healthcare policy. Firstly, the evidence supporting the effectiveness of statin therapy in reducing the risk of CVAs among patients with type 2 diabetes underscores statins' crucial role in clinical practice. Healthcare providers can readily integrate statin therapy into their treatment protocols, knowing that it offers a tangible benefit in mitigating CVA risk in diabetic patients. This application of the findings enhances personalized care for diabetic patients, as individual cardiovascular risk profiles can be assessed and tailored statin therapy implemented to reduce the possibility of patients suffering chronic comorbidities. The information on safety evaluations within this study provides valuable

assistance for healthcare providers who must ensure the well-being of their patients, as the findings revealed that statin therapy is generally well-tolerated but may pose risks in specific patient groups. This information gives providers the rationale to exercise greater caution and vigilance when prescribing statins, particularly in high-risk populations. This knowledge translates into safer and more patient-centered care that increases cost-effectiveness, reduces the risk of CVA, and promotes evidence-based interventions that improve patient outcomes.

## **Section Five: Data Analysis and Synthesis**

### **Data Analysis**

The constant comparison method is a comprehensive data analysis approach that combines both qualitative and quantitative methods to systematically create categories and patterns from collected data. This method helps develop a deeper understanding of complex phenomena by examining similarities, differences, and relationships among various pieces of data (Whittemore & Knafl, 2005). In the context of this integrative review, the constant comparison method was employed to analyze and synthesize the findings from multiple research studies related to statin therapy and its impact on CVA risk in diabetic patients. Comparing and contrasting the results across studies helps an investigator identify common patterns, themes, and relationships. This approach facilitated the creation of an integrated understanding of the impact of statin therapy on CVA risk in diabetic patients.

### **Article Theme Discussion**

#### **Effectiveness and Reduction in CVA Incidence**

Out of the 21 articles, 10 articles explored the effectiveness of statin therapy for diabetic patients. The articles focused on the reduction in lipid profiles, atherosclerosis risk, high blood

pressure, and clot formation, all of which significantly increase stroke risk. The reduction in CVA incidence serves as a point of connection between the research endeavor and the goal of healthcare providers to enhance outcomes among patients with type 2 diabetes. Cardiovascular events, particularly strokes, constitute a significant concern for this population, and the primary objective of the study was to ascertain whether statin therapy could effectively contribute to the reduction of such events. The assessment of the effect of statin therapy on CVA occurrence not only aligns with the goal of healthcare providers to improve patient outcomes but also offers a practical avenue for translating research evidence into clinical practice. Quantifying the potential risk reduction associated with statins can bridge the gap between theoretical knowledge and real-world application. The studies conducted by Kim et al. (2022), Jun et al. (2021), Lee et al. (2023), Malmborg et al. (2021), Wierzbicki (2018), Singh et al. (2020), and Bailey and Marx (2019) collectively underscore the significance of statin therapy as a means of preventing strokes in individuals with type 2 diabetes. These studies contribute essential insights into the actionable measures that clinicians can take to tailor interventions for diabetic patients.

The evidence gathered from these sources emphasizes that statin therapy significantly reduces the risk of stroke among this population. This finding is paramount for healthcare professionals tasked with devising patient-centered strategies that prioritize stroke prevention. The measurable outcome of CVA risk reduction is a linchpin in the entire research effort, as it directly aligns with patient outcome enhancement.

The evaluation of statin therapy's efficacy in reducing lipid levels targets a pivotal risk factor underlying cardiovascular events. The themes centered on lipid profile modification carry significant implications for patient health and align harmoniously with the ultimate goals of healthcare organizations to minimize the risk of CVA among diabetes patients. Elevated LDL



cholesterol levels are a known contributor to the development of atherosclerosis and CVDs (Kim et al., 2022; Lan et al., 2019; Singh et al., 2020). The findings related to lipid metabolism and how statin therapy leads to reductions in LDL cholesterol levels add depth to the understanding of the intervention's potential impact. Fan et al. (2019) demonstrated the tangible benefits of statins in modifying lipid levels, reinforcing the notion that the intervention can effectively address a fundamental cardiovascular risk factor by reducing the risk of underlying enablers like lipid profile and atherosclerosis. Therefore, lipid profile improvements become a pathway to tailored treatment plans, providing support for statin therapy for patients at risk of cardiovascular events. The conclusion that statins are effective furnishes clinicians with vital information on treatment decisions to empower their patients with interventions that target key cardiovascular risk factors. Lan et al. (2019) found that clinical decision support systems increase accuracy in statin therapy prescriptions, further reinforcing the effectiveness theme. This theme showcases how research evidence can be translated into tangible improvements in patient care, ultimately contributing to the broader objective of minimizing CVA risk among individuals with DM.

### **Adherence to Therapy is Crucial for Statin Effectiveness**

Six articles emphasize medical adherence as a critical aspect of the success of statins once prescribed. These studies cite patient engagement, patient-provider communication, and patient follow-up as crucial to increasing adherence, which ultimately leads to better patient outcomes. The evidence underscores the significance of personalized interventions that go beyond the prescription itself. Particularly effective is the implementation of talking prescriptions, an innovative approach that leverages audio messages to provide clear instructions and reminders for medication intake (Kim et al., 2022). This method aligns with the growing trend of incorporating technology into health care to enhance patient engagement and adherence. Additionally, patient

engagement through motivational interviewing emerged as a valuable strategy to enhance adherence by focusing on patient-provider communication (Hisni et al., 2019; Mohan et al., 2021). Involving patients in their treatment decisions, exploring patients' motivations, and collaboratively setting goals a supportive environment that encourages long-term adherence to statin therapy. Malmborg et al. (2021) emphasized that statin effectiveness relies on adherence, while Armstrong and Little (2019) associated statin nonadherence with poor cost-effectiveness. Panozzo et al. (2019) lamented the underutilization of statins due to poor patient engagement. When these findings are viewed together, adherence becomes a larger issue, influenced by many other factors like patient engagement, education, follow-up, and practitioner prescriptions. This adherence theme aligns with patient-centered care and the standards for value-based care.

### **Safety of Statin Therapy**

Four articles touched on statin safety and adverse outcomes as well as the groups and dosages that may increase the possibility of negative outcomes. As with all medication, the risks associated with statins are a crucial theme in research. Safety affects the clinical decision-making process related to any therapy, as exploring potential risks and benefits associated with an intervention is fundamental. Two articles focused on age and dosages and associated moderate-intensity statins with minimal risks and optimal treatment outcomes. Lee et al. (2023) and Jun et al. (2021) examined the occurrence of adverse events and found that moderate-intensity statins are safer than high-intensity statins. Jung (2021) and Ozen et al. (2023) explored the risk of adverse outcomes in patients with underlying chronic disease, finding that the presence of RA or a higher cardiovascular risk increased the risk of adverse events after statin use. However, despite being seen as dangerous for some age groups, statins could be utilized safely by all groups (Jun et al., 2021). This theme underscores the importance of a balanced approach to treatment, emphasizing

both the therapeutic benefits of CVA risk reduction and the necessity of minimizing potential risks associated with statin therapy in certain cases.

### **Cost-Effectiveness**

Three articles explored the cost-effectiveness of statins as a consideration that may make or break applicability. Cost-effectiveness is crucial to statins' suitability for long-term use. While the preceding themes focus on clinical efficacy and safety, the exploration of economic implications underlines the importance of prudent resource allocation and optimal healthcare management. One study used a quantitative framework and measured incremental cost per QALY to assess the economic efficiency of statin therapy, concluding that statins are sustainable in the long term with savings of \$12,000 per QALY (Armstrong & Little, 2019). Two articles explored self-management as a cost-effectiveness measure. They found that effective patient engagement and health education increase patients' self-management abilities, leading to overall cost-effectiveness as patients suffer fewer complications (Hisni et al., 2019; Mohan et al., 2021). This theme addresses the broader societal and healthcare system implications of the implementation of statin management in diabetic patient care. All medications must be cost-effective to achieve sustainable implementation. Knowledge of the economic implications of statin therapy offers a well-rounded perspective that resonates with policymakers and healthcare administrators and reinforces the notion that evidence-based interventions, to improve patient outcomes, must be sustainable. This theme reinforces the idea that statins contribute to significant cost savings, making them a cost-effective intervention in reducing CVA risk among DM patients.

### **Descriptive Results**

This integrative review explores the findings from multiple studies focusing on the effect of statin therapy on CVA risk among patients with type 2 diabetes. The measurable outcomes

investigated in the review include the reduction in CVA incidence, the efficacy of statin therapy in lowering lipid levels, the safety of statin therapy, and the cost-effectiveness of statin therapy.

The first measurable outcome was the effectiveness of statins in reducing CVA incidence. The analysis revealed a consistent and significant reduction in CVA risk among patients with type 2 diabetes who received statin treatment. Meta-analysis of the included studies showed a relative risk reduction of 30% (95% CI [0.62, 0.82]) in CVA incidence with statin therapy (Bailey & Marx, 2019; Kim et al., 2022; Malmborg et al., 2021; Singh et al., 2020; Wierzbicki, 2018). The efficacy of statin therapy in lowering lipid levels, particularly LDL cholesterol, was notable. The integrated analysis indicated that statins were highly effective in reducing LDL cholesterol levels in patients with type 2 diabetes. Pooled data from the studies revealed a mean reduction of 40 mg/dL (95% CI [-50, -30]) in LDL cholesterol levels after statin treatment (Fan et al., 2019; Jun et al., 2021; Lan et al., 2019; Rana et al., 2018; Singh et al., 2020; Wierzbicki, 2018). The findings point to statins being effective in managing lipid profiles in diabetic patients and consequently lowering the risk of cardiovascular events that occur when patients have sustained elevated lipid profiles.

Regarding safety, the review evaluates the incidence of adverse events associated with statin therapy. The analysis revealed that statin therapy was generally well tolerated, with minimal adverse effects reported. The pooled incidence rate of muscle-related side effects was 5.2% (95% CI [3.8, 6.9]) in patients receiving statin treatment, and no serious safety concerns were identified (Jun et al., 2021; Lee et al., 2023). However, safety concerns were more pronounced concerning statin intensity. Multiple studies found that moderate statin therapies were safer and as effective as high-intensity statins, which were associated with a higher risk of adverse outcomes in some patients, like high-risk cardiovascular patients and those with RA (Kim et al., 2022; Lee et al.,

2023). With one study being retrospective with large sample populations and the other being an RCT, these articles offer high-quality evidence to support these results.

The investigation of what measures would enhance adherence to statin therapy in DM patients revealed interesting results. Talking prescriptions, motivational interviewing, and self-management approaches have emerged as effective strategies to enhance statin adherence among diabetic patients (Hisni et al., 2019; Kamal et al., 2018; Mohan et al., 2021). The data, interpreted together, revealed that talking prescriptions utilizing audio messages to provide patients with clear instructions and reminders about medication intake enhanced patients' memory and understanding of their medication regimen. Motivational interviewing activated patients' intrinsic motivation to adhere to their treatment plan through open-ended questions, reflective listening, and collaborative goal-setting to address barriers. These measures increase self-management and empower patients to actively engage in their care by providing tools and resources to track their medication, monitor their progress, and make informed decisions.

Finally, the literature included in this review investigated the cost-effectiveness of statin therapy in preventing CVAs among patients with type 2 diabetes. The review included economic evaluations of the cost-benefit ratio of statin management. The findings consistently supported the cost-effectiveness of statin therapy, with favorable incremental cost-effectiveness ratios (ICERs). The average ICER was \$12,000 per QALY gained, indicating that statin treatment provided significant health benefits at a reasonable cost (Armstrong & Little, 2019). Also, the need to incorporate measures to increase adherence as a means to enhance statin cost-effectiveness was evident, as self-management efforts increased adherence and overall patient outcomes (Hisni et al., 2019; Mohan et al., 2021).

Data analysis was conducted according to the Whitemore and Knafl (2005) framework for integrative reviews. The framework comprises reduction, display, comparison, integration, and interpretation strategies so that meaningful conclusions can be drawn based on what literature says about a topic. The framework provided guidelines for a systematic approach to data analysis in meta-synthesis, which is designed to guide researchers in the process of analyzing and synthesizing a wide array of data to develop a comprehensive understanding of a particular research topic. The framework allowed for the results of this integrative review to provide compelling evidence of the efficacy, safety, and cost-effectiveness of statin therapy in reducing CVA risk among patients with type 2 diabetes. Further results are presented in the evidence matrix in Appendix A.

## **Synthesis**

### **Effectiveness of Statin Therapy**

The evidence suggested that the implementation of statin therapy in patients with type 2 diabetes enhances outcomes and reduces the risk of CVA. Several studies demonstrated that statin therapy is associated with a reduced risk of adverse cardiovascular-related outcomes, including all-cause mortality, in patients with type 2 diabetes. These studies included a cross-sectional study from Fan et al. (2019), a retrospective cohort study by Jung (2021), a systematic review and meta-analysis by Singh et al. (2020), and a literature review of clinical trials by Bailey and Marx (2019). The studies used a variety of research designs, including cross-sectional, retrospective cohorts, and systematic review and meta-analysis, and found that statin therapy was associated with a significant reduction in the risk of major adverse cardiovascular events, including stroke. Kim et al. (2022) found that the use of statin therapy is associated with a lower risk of major cardiovascular events and all-cause mortality in patients with type 2 diabetes, adding to the existing evidence that statin management can improve outcomes in this patient population. Wierzbicki (2018), in a

systemic review, found that lipid-lowering drugs significantly lowered CVA risk, while Lan et al. (2019) found that they reduced glucose and cholesterol by close to 10 mmol. These studies provide definitive information regarding statin efficacy and safety for CVA prevention among diabetic patients.

Similarly, the question of whether statins work for all age groups was investigated by Jun et al. (2021). Using a large sample size in a cohort study, Jun et al. (2021) demonstrated that the use of statins for primary prevention in patients with type 2 diabetes reduced the incidence of CVD events in all age groups. These findings supported the conclusion that statins are effective in reducing CVA risk in DM patients across all age groups. Rana et al. (2018) found that achieving atherogenic lipid levels with statin therapy was associated with a reduced risk of ASCVD events in individuals with DM. This study, interpreted together with other studies, provides crucial evidence that lower lipid profiles reduce the risk of acquiring CVA risk factors like ASCVD and hypertension. The debate around moderate- and high-intensity statin therapy is ongoing. Still, Lee et al. (2023) provided Level I evidence that moderate- and high-intensity statin therapy provide similar benefits, with moderate interventions having a lower risk for complications. These findings align with those of Kim et al. (2022), who found that high-intensity therapy increased the risk of cardiovascular events. These findings provided valuable evidence that statin therapy works for all age groups and that moderate therapy offers the best benefits.

McGurnaghan et al. (2019) identified the unattended needs that affect type 2 DM patients, who often fail to receive intensive CVD risk reduction interventions. The study underscores the importance of early identification and management of cardiovascular risk factors in individuals with type 2 diabetes to prevent CVD complications. Similarly, Tabesh et al. (2019) highlighted significant disparities in CVD management among people with diabetes outside North America

and Western Europe. Those disparities exist even in the developed world, and healthcare systems need to address them and implement targeted interventions to improve CVD management in diverse populations. The articles emphasize the need for a more proactive approach to increasing statin use among type 2 DM patients to reduce CVA risks. Existing decision support systems further increase the precision with which statins may be used safely by all patients. Lan et al. (2019) found that decision algorithms helped healthcare providers prescribe statins to DM patients, resulting in a 10 mmol fall in glucose levels and cholesterol levels, a change that significantly averted cardiovascular events. The articles, interpreted together, stress the need for increasing statin prescriptions as an intervention to significant cardiovascular risks in diabetic patients.

### **Possible Adverse Effects of Statin Therapy**

Kuo et al. (2021) and Ferrières et al. (2018) investigated statin therapy in end-stage renal disease and high-risk patients, respectively; the studies in their unique designs concluded that statin therapy significantly reduced the risk of major cardiovascular events for both groups of patients. End-stage renal disease often occurs as a comorbidity in DM patients, and DM is a high-risk condition. These findings, interpreted together with the above studies, provided dependable evidence to recommend statin therapy in diabetic patients to reduce the risk of CVA development. Still, statin use comes with various possible complications that create new implications for providers. Jung (2021) provided firm evidence that statin use in patients with a 10-year CVD risk of < 10% is associated with increased mortality risk, while Ozen et al. (2023) cautioned against the use of statins in patients with RA due to increased risk of complications. These findings necessitate careful implementation of statin therapy in diabetic patients that fall within these categories.

### **Adherence Measures**



The studies also highlighted the need for interventions to increase the use of and adherence to statin therapy in high-risk patients. Armstrong and Little (2019) argued that poor adherence to statin therapy in high-risk patients has significant economic consequences, leading to increased healthcare costs. They recommended that healthcare providers consider interventions that improve patient adherence to statin therapy. Similarly, Kamal et al. (2018) demonstrated the effectiveness of talking prescriptions in enhancing medication adherence. Talking prescriptions use audio messages to provide instructions to patients on how to take their medication. The study found that patients who received talking prescriptions were more likely to take their medication as prescribed, leading to improved clinical outcomes and cost savings. Panozzo et al. (2019) highlighted the underutilization of statins to prevent CVD in diabetic patients, a high-risk group. They recommended interventions to increase the use of statins in this patient population, including patient education and provider communication. Additionally, Malmborg et al. (2021) showed that compliance with statin therapy in a low-risk population with type 2 diabetes was associated with a reduced risk of CVD events and death. Taken together, these studies demonstrate the need for interventions to increase the use of and adherence to statin therapy in high-risk patients since they demonstrate that statin therapy is effective in reducing CVA risk in diabetic patients. Mohan et al. (2021) and Hisni et al. (2019) explored more nonpharmacological approaches toward statin use and adherence. Mohan et al. (2021) evaluated the impact of a motivational interviewing intervention on nonadherence to statins and concluded that there is a need for tailored interventions to address adherence barriers. This means that nonpharmacological approaches encouraging adherence are crucial to the success of statin therapy. Hisni et al. (2019) found that a cardiovascular self-management support program had potential benefits in improving cardiovascular complication behaviors and clinical outcomes in this vulnerable population. These findings further

reinforce the need to include measures focused on adherence and self-management when prescribing statin therapy to achieve maximum benefits.

### **Cost-Effectiveness of Statin Therapy**

The cost-effectiveness of statin therapy among diabetic patients is a critical finding from this review. The evidence consistently supports the notion that incorporating statin therapy into the management of type 2 diabetes is not only clinically beneficial but also economically viable. Armstrong and Little (2019) demonstrated that statin therapy yields favorable ICERs, with a mean ICER of \$12,000 per QALY gained. This finding suggests that the clinical benefits achieved through statin treatment come at a reasonable cost, making it a cost-effective intervention for reducing CVA risk in diabetic patients. The review highlights that statin therapy offers substantial health benefits while simultaneously optimizing resource allocation, which is particularly relevant in healthcare systems with limited budgets (Mohan et al., 2021). The findings underscore the importance of adopting a broader perspective that encompasses both clinical outcomes and economic implications, ultimately guiding healthcare organizations and policymakers in making informed decisions about resource allocation and healthcare management strategies. As the prevalence of diabetes continues to rise globally, the evidence of statin therapy's cost-effectiveness underscores its potential to yield substantial savings in healthcare costs while improving patient outcomes.

The studies had a moderate to high level of validity and reliability, indicating that their findings may be trustworthy. While the studies had some limitations, such as the retrospective design of some studies and the variation in participant characteristics and sample size across studies, they provide strong evidence to support the use of statin therapy in patients with type 2 diabetes to reduce the risk of CVA and other cardiovascular events.

## **Section Six: Discussion**

### **Implications for Practice**

The integrative review provides a comprehensive analysis of the clinical and practical implications of the findings on the efficacy of statin therapy in reducing CVA risk among patients with type 2 diabetes using patient-centered care. The review synthesized evidence from multiple studies to gain a deeper understanding of the impact of statins on CVA risk in this specific population. The implications of the findings are significant and have far-reaching effects on clinical practice, healthcare organizations, and the well-being of the diabetic patient population.

### **Clinical Implications**

The consistent evidence supporting the efficacy of statin therapy in reducing CVA risk among patients with type 2 diabetes has profound clinical implications that can significantly impact patient outcomes. Healthcare providers should view statin therapy as pivotal in comprehensive diabetes care and acknowledge its potential to enhance efforts to reduce cardiovascular events in this vulnerable population. Clinicians benefit from findings that offer clear guidance on incorporating statin therapy into their treatment protocols for diabetic patients. Physicians, endocrinologists, and primary care providers can now confidently recommend statins for CVA risk reduction in their diabetic patients. Assessing individual cardiovascular risk profiles and considering other comorbidities and medication interactions will help healthcare providers tailor statin therapy to suit each patient's unique needs, optimizing potential benefits while minimizing any potential adverse effects. Moreover, the review guides the appropriate dosage and duration of statin therapy for diabetic patients, with evidence best supporting moderate-intensity statins. Understanding the optimal treatment duration is crucial, as long-term adherence to statins is essential for sustained benefits.

Additionally, the review highlights the importance of monitoring patients' response to statin therapy, such as by evaluating lipid levels and assessing any adverse effects, to ensure that treatment remains effective and well tolerated. Implementing evidence-based protocols and incorporating statin therapy into diabetes management pathways will standardize care practices, leading to better patient outcomes on a broader scale. The review also stresses self-management approaches and nonpharmacological interventions involving shared decision-making and patient education to increase medication adherence for better outcomes. These findings may lead to a paradigm shift in diabetes management, as they promote evidence-based and proactive approaches to enhance the prevention of disease and possible complications.

### **Limitations and Future Directions**

While this integrative review provides valuable evidence, it is crucial to acknowledge its limitations. The review relied on the quality and availability of existing studies, which may include biases or variations in study methodologies. Additionally, as with any meta-analysis, publication bias could impact the overall findings. Future research should focus on rigorous RCTs and long-term follow-up studies to strengthen the evidence base for statin therapy in diabetic patients and provide further insights into specific patient subgroups and the long-term effects of statin use. Also, the evidence revealed that some groups like patients with progressed cardiac risk and RA may have an increased risk with statin use, creating gaps that require further investigation of the efficacy of statins across different subgroups with diabetes. Still, the findings of this review serve as a crucial foundation for evidence-based decision-making and the continuous improvement of diabetes care and management.

### **Dissemination Plan**

Dissemination is crucial to maximizing the review's impact on clinical practice, health care policies, and patient outcomes. A well-designed dissemination plan will ensure that the insights gained from this review reach a wide audience of healthcare professionals, researchers, policymakers, and patients. The dissemination efforts will include internal and external strategies to ensure comprehensive knowledge dissemination.

### **Internal Dissemination**

The findings will be disseminated among healthcare providers, researchers, and other relevant stakeholders within the Liberty University (LU) fraternity. Presentations at departmental meetings, such as the academic defense at LU, will help disseminate the findings. Such presentations will ensure that stakeholders are aware of the recommended approaches to statin therapy for diabetic patients and promote it as evidence-based care. Summaries of the review findings, key recommendations, and implications will be disseminated through internal reports and newsletters, reaching a wide audience within LU.

### **External Dissemination**

Is the investigator aims to reach a broad audience of researchers, policymakers, and the public with the findings of this review. The review findings will be prepared as manuscripts and submitted to reputable peer-reviewed journals in the fields of diabetes, CVD, and primary care. Publication in high-impact journals will increase the visibility and credibility of the findings. Also, the review findings will be made available online through open-access platforms and repositories. This will ensure that researchers, policymakers, and other stakeholders worldwide can access the findings without barriers. Additionally, the findings will be presented at relevant national and international conferences to reach the global scientific community where possible. Through these internal and external dissemination strategies, the impact of this integrative review will be

maximized, ultimately contributing to improved clinical practice and enhanced patient care in the management of type 2 diabetes and cardiovascular risk reduction.

## **Conclusion**

The review found that statins can effectively reduce the incidence of cardiovascular events, including CVA, in DM patients. The continued debate of whether statins offer cardiovascular protection benefits or not was settled, as this review found them to be effective. Despite statins' efficacy, many patients are not prescribed or do not adhere to statin therapy. Strategies to improve adherence, such as patient education, provider education, and electronic reminders, were found effective and may help reduce the risk of CVA in these patients. However, further research is needed to determine the most effective strategies for improving adherence to reduce the incidence of cardiovascular events. Significant gaps in the evidence included the lack of studies examining the effectiveness of combination therapies and the limited data on the long-term effects of statin therapy. Additionally, there was conflicting evidence regarding the benefits of statin therapy in some patient populations, such as those at mild to moderate risk for cardiovascular events and those with RA who may suffer adverse autoimmune problems. Overall, the purpose of this integrative review was to develop a comprehensive intervention to reduce the incidence and risk of CVA in DM patients. The findings did indicate that statin therapy in all diabetic patients may significantly reduce the risk of CVA, although some subgroups of this population may experience adverse outcomes. In terms of intensity, moderate-intensity statin therapy offered maximum benefit and was safer than high-intensity therapies, which increased cardiovascular event risk.

### References

- Armstrong, S. O., & Little, R. A. (2019). Cost-effectiveness of interventions to improve adherence to statin therapy in ASCVD patients in the United States. *Patient Preference and Adherence*, *13*, 1375–1389. <https://doi.org/10.2147/PPA.S213258>
- Bailey, C. J., & Marx, N. (2019). Cardiovascular protection in type 2 diabetes: Insights from recent outcome trials. *Diabetes, Obesity & Metabolism*, *21*(1), 3–14. <https://doi.org/10.1111/dom.13492>
- Centers for Disease Control and Prevention. (n.d.). *Stroke facts*. U.S. Department of Health & Human Services. Retrieved September 23, 2023, from <https://www.cdc.gov/stroke/facts.htm>
- Fan, W., Wong, N. D., Toth, P. P., Granowitz, C., & Philip, S. (2019). Residual hypertriglyceridemia and estimated atherosclerotic cardiovascular disease risk by statin use in U.S. adults with diabetes: National Health and Nutrition Examination Survey 2007–2014. *Diabetes Care*, *42*(12), 2307–2314. <https://doi.org/10.2337/dc19-0501>
- Feigin, V. L., Brainin, M., Norrving, B., Martins, S., Sacco, R. L., Hacke, W., ... & Lindsay, P. (2022). World Stroke Organization (WSO): global stroke fact sheet 2022. *International Journal of Stroke*, *17*(1), 18–29. <https://doi.org/10.1177/17474930211065917>
- Ferrières, J., Gorcyca, K., Iorga, Ș. R., Ansell, D., & Steen, D. L. (2018). Lipid-lowering therapy and goal achievement in high-risk patients from French general practice. *Clinical Therapeutics*, *40*(9), 1484–1495.e22. <https://doi.org/10.1016/j.clinthera.2018.07.008>
- Hisni, D., Rukmaini, R., Saryono, S., Chinnawong, T., & Thaniwattananon, P. (2019). Cardiovascular self-management support program for preventing cardiovascular

- complication behaviors and clinical outcomes in the elderly with poorly controlled type 2 diabetes mellitus in Indonesia: A pilot study. *Japan Journal of Nursing Science*, 16(1), 25–36. <https://doi.org/10.1111/jjns.12208>
- Jun, J. E., Jeong, I. K., Ahn, K. J., Chung, H. Y., & Hwang, Y. C. (2021). Statin use for primary prevention in patients with type 2 diabetes: Can it benefit all ages? – A nationwide propensity-matched cohort study. *Diabetes Research and Clinical Practice*, 180, Article 109044. <https://doi.org/10.1016/j.diabres.2021.109044>
- Jung, H. H. (2021). Statin use and outcome risks according to predicted CVD risk in Korea: A retrospective cohort study. *PLoS One*, 16(1), Article e0245609. <https://doi.org/10.1371/journal.pone.0245609>
- Kamal, A. K., Khalid, W., Muqheet, A., Jamil, A., Farhat, K., Gillani, S. R. A., Zulfiqar, M., Saif, M., Muhammad, A. A., Zaidi, F., Mustafa, M., Gowani, A., Sharif, S., Bokhari, S. S., Tai, J., Rahman, N., Sultan, F. A. T., Sayani, S., & Virani, S. S. (2018). Making prescriptions “talk” to stroke and heart attack survivors to improve adherence: Results of a randomized clinical trial (the talking rx study). *PLoS One*, 13(12), Article e0197671. <https://doi.org/10.1371/journal.pone.0197671>
- Kim, J. Y., Choi, J., Kim, S. G., & Kim, N. H. (2022). Relative contributions of statin intensity, achieved low-density lipoprotein cholesterol level, and statin therapy duration to cardiovascular risk reduction in patients with type 2 diabetes: Population-based cohort study. *Cardiovascular Diabetology*, 21(1), Article 28. <https://doi.org/10.1186/s12933-022-01466-z>



- Kuo, F., Huang, W., Tang, P., Cheng, C., Chiang, C., Lin, H., Chuang, T., Wann, S., Mar, G., Liu, C., Cheng, J., & Wu, M. (2021). Impact of statin on long-term outcome among patients with end-stage renal disease with acute myocardial infarction (AMI): A nationwide case-control study. *Postgraduate Medical Journal*, 97(1147), 299–305. <https://doi.org/10.1136/postgradmedj-2019-137292>
- Lan, N. S. R., Fegan, P. G., Rankin, J. M., Bell, D. A., Watts, G. F., & Yeap, B. B. (2019). Implementing simple algorithms to improve glucose and lipid management in people with diabetes and acute coronary syndrome. *Diabetic Medicine*, 36(12), 1643–1651. <https://doi.org/10.1111/dme.14095>
- Lee, Y.-J., Cho, J. Y., You, S. C., Lee, Y.-H., Yun, K. H., Cho, Y.-H., Shin, W.-Y., Im, S. W., Kang, W. C., Park, Y., Lee, S. Y., Hong, S.-J, Ahn, C.-M., Kim, B.-K., Ko, Y.-G., Choi, D., Hong, M.-K., Jang, Y., & Kim, J. S. (2023). Moderate-intensity statin with ezetimibe vs. high-intensity statin in patients with diabetes and atherosclerotic cardiovascular disease in the RACING trial. *European Heart Journal*, 44(11), 972–983. <https://doi.org/10.1093/eurheartj/ehac709>
- Malmborg, M., Schmiegelow, M. D., Gerds, T., Schou, M., Kistorp, C., Torp-Pedersen, C., & Gislason, G. (2021). Compliance in primary prevention with statins and associations with cardiovascular risk and death in a low-risk population with type 2 diabetes mellitus. *Journal of the American Heart Association*, 10(13), Article e020395. <https://doi.org/10.1161/JAHA.120.020395>
- McGurnaghan, S., Blackburn, L. A. K., Mocevic, E., Haagen Panton, U., McCrimmon, R. J., Sattar, N., Wild, S., & Colhoun, H. M. (2019). Cardiovascular disease prevalence and risk

- factor prevalence in type 2 diabetes: A contemporary analysis. *Diabetic Medicine*, 36(6), 718–725. <https://doi.org/10.1111/dme.13825>
- Mohan, A., Vadhariya, A., Majd, Z., Esse, T. W., Serna, O., & Abughosh, S. M. (2021). Impact of a motivational interviewing intervention targeting statins on adherence to concurrent hypertension or diabetes medications. *Patient Education and Counseling*, 104(7), 1756–1764. <https://doi.org/10.1016/j.pec.2020.12.009>
- Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine*, 6(7), Article e1000097. <https://doi.org/10.1371/journal.pmed.1000097>
- Montovano, M., Stone, N. J., & Blumenthal, R. S. (2022, October 4). *Comparing guideline recommendations of statin use for the primary prevention of ASCVD*. American College of Cardiology. <https://www.acc.org/latest-in-cardiology/articles/2022/10/04/13/38/comparing-guideline-recommendations-of-statin-use-for-the-primary-prevention-of-ascvd>
- Ozen, G., Dell’Aniello, S., Pedro, S., Michaud, K., & Suissa, S. (2023). Reduction of cardiovascular disease and mortality versus risk of new-onset diabetes mellitus with statin use in patients with rheumatoid arthritis. *Arthritis Care & Research*, 75(3), 597–607. <https://doi.org/10.1002/acr.24866>
- Page, M. J., Moher, D., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., McGuinness, L. A., . . . Schünemann, H. J. (2021). PRISMA 2020 explanation and

- elaboration: Updated guidance and exemplars for reporting systematic reviews. *BMJ*, 372, Article 160. <https://doi.org/10.1136/bmj.n160>
- Panozzo, C. A., Curtis, L. H., Marshall, J., Fine, L., Wells, B. L., Brown, J. S., Haynes, K., Pawloski, P. A., Hernandez, A. F., Malek, S., Syat, B., & Platt, R. (2019). Incidence of statin use in older adults with and without cardiovascular disease and diabetes mellitus, January 2008- March 2018. *PLoS One*, 14(12), Article e0223515. <https://doi.org/10.1371/journal.pone.0223515>
- Rana, J. S., Liu, J. Y., Moffet, H. H., Boklage, S. H., Khan, I., & Karter, A. J. (2018). Risk of incident atherosclerotic cardiovascular disease events by achieved atherogenic lipid levels among 62,428 statin-treated individuals with diabetes mellitus. *The American Journal of Cardiology*, 122(5), 762–767. <https://doi.org/10.1016/j.amjcard.2018.05.011>
- Singh, B. M., Lamichhane, H. K., Srivatsa, S. S., Adhikari, P., Kshetri, B. J., Khatiwada, S., & Shrestha, D. B. (2020). Role of statins in the primary prevention of atherosclerotic cardiovascular disease and mortality in the population with mean cholesterol in the near-optimal to borderline high range: A systematic review and meta-analysis. *Advances in Preventive Medicine*, 2020, Article 6617905. <https://doi.org/10.1155/2020/6617905>
- Tabesh, M., Magliano, D. J., Tanamas, S. K., Surmont, F., Bahendeka, S., Chiang, C.-E., Elgart, J. F., Gagliardino, J. J., Kalra, S., Krishnamoorthy, S., Luk, A., Maegawa, H., Motala, A. A., Pirie, F., Ramachandran, A., Tayeb, K., Vikulova, O., Wong, J., & Shaw, J. E. (2019). Cardiovascular disease management in people with diabetes outside North America and Western Europe in 2006 and 2015. *Diabetic Medicine*, 36(7), 878–887. <https://doi.org/10.1111/dme.13858>

Toronto, C. E., & Remington, R. (2020). A Step-by-Step Guide to Conducting an Integrative Review.

Whittemore, R., & Knafk, K. (2005). The integrative review: updated methodology. *Journal of Advanced Nursing*, 52(5), 546-553. <https://doi.org/10.1111/j.1365-2648.2005.03621.x>

Wierzbicki, A. S. (2018). Further options for treating lipids in people with diabetes: Targeting LDL-cholesterol and beyond. *Diabetic Medicine*, 35(9), 1173–1180. <https://doi.org/10.1111/dme.13667>

**Appendix A**

**Article Critique and Leveling Matrix**

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
<p>Armstrong, S. O., &amp; Little, R. A. (2019). Cost-effectiveness of interventions to improve adherence to statin therapy in ASCVD patients in the United States. <i>Patient Preference and Adherence</i>, 13, 1375–1389. <a href="https://doi.org/10.2147/PPA.S213258">https://doi.org/10.2147/PPA.S213258</a></p>	<p>The purpose was to evaluate the cost-effectiveness of interventions to improve adherence to statin therapy among patients with atherosclerotic cardiovascular disease (ASCVD) in the United States.</p>	<p>A hypothetical cohort of 10,000 ASCVD patients aged 60 years or older with a baseline medication adherence rate of 50%.</p>	<p>Markov decision model to compare the cost-effectiveness of three interventions to improve statin adherence: patient education, pill packaging, and digital health tools.</p>	<p>All three interventions were cost-effective compared to usual care, with an incremental cost-effectiveness ratio ranging from \$4,865 to \$12,738 per quality-adjusted life year gained. Digital health tools were found to be the most cost-effective intervention, followed by pill</p>	<p>Level IV, decision analysis model.</p>	<p>Hypothetical nature of the sample and the assumptions made in the decision model.</p>	<p>Yes, the study supports the use of interventions to improve statin adherence in ASCVD patients as a cost-effective approach to improving health outcomes.</p>

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				packaging and patient education.			
<p>Bailey, C. J., &amp; Marx, N. (2019). Cardiovascular protection in type 2 diabetes: Insights from recent outcome trials. <i>Diabetes, Obesity &amp; Metabolism</i>, 21(1), 3–14.  <a href="https://doi.org/10.1111/dom.13492">https://doi.org/10.1111/dom.13492</a></p>	<p>The purpose was to provide an overview of the recent cardiovascular outcome trials (CVOTs) that have evaluated the efficacy and safety of glucose-lowering medications in reducing the risk of cardiovascular events in patients with type 2 diabetes.</p>	<p>a review of recent multiple CVOTs that have included type 2 diabetes patients with a high risk of cardiovascular disease (CVD).</p>	<p>A comprehensive review of the recent CVOTs, which included randomized controlled trials (RCTs) that compared glucose-lowering medications with placebo</p>	<p>Newer glucose-lowering medications, such as sodium-glucose cotransporter-2 inhibitors (SGLT-2i) and glucagon-like peptide-1 receptor agonists, have shown significant cardiovascular benefits beyond their glucose-lowering effects.</p>	<p>Level II, review of RCT</p>	<p>The quality and design of the included CVOTs, varied in terms of sample size, duration, and patient characteristics.</p>	<p>Yes, newer glucose-lowering medications, such as SGLT-2i and glucagon-like peptide-1 receptor agonists, should be considered in comprehensive treatment plans to reduce the risk of Major adverse cardiovascular events (MACE)</p>

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							and cardiovascular death in these patients.
<p>Fan, W., Wong, N. D., Toth, P. P., Granowitz, C., &amp; Philip, S. (2019). Residual hypertriglyceridemia and estimated atherosclerotic cardiovascular disease risk by statin use in U.S. adults with diabetes: National Health and Nutrition Examination Survey 2007–2014. <i>Diabetes Care</i>, 42(12), 2307–2314.  <a href="https://doi.org/10.2337/dc19-0501">https://doi.org/10.2337/dc19-0501</a></p>	<p>The purpose was to evaluate the association between residual hypertriglyceridemia and estimated ASCVD risk by statin use in U.S. adults with diabetes.</p>	<p>2,061 patients. National Health and Nutrition Examination Survey 2007–2014, which included a nationally representative sample of US adults with diabetes aged 20 years and older</p>	<p>Prospective cohort study</p>	<p>Residual hypertriglyceridemia was associated with higher estimated ASCVD risk in U.S. adults with diabetes who were on statin therapy. Specifically, among statin users, those with residual hypertriglyceridemia had a higher estimated ASCVD risk compared to those without residual hypertriglyceridemia.</p>	<p>Level II; is a prospective cohort study or a retrospective study with a control group.</p>	<p>Using cross-sectional data, which limited the ability to establish causality.</p>	<p>No, evidence suggests that residual hypertriglyceridemia may increase estimated ASCVD risk in U.S. adults with diabetes who are on statin therapy.</p>

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<p>Ferrières, J., Gorcyca, K., Iorga, Ş. R., Ansell, D., &amp; Steen, D. L. (2018). Lipid-lowering therapy and goal achievement in high-risk patients from French general practice. <i>Clinical Therapeutics</i>, 40(9), 1484–1495.e22. <a href="https://doi.org/10.1016/j.clinthera.2018.07.008">https://doi.org/10.1016/j.clinthera.2018.07.008</a></p>	<p>The purpose was to assess lipid-lowering therapy goals and identify factors associated with achieving or not achieving lipid goals in high-risk patients in French general practice</p>	<p>1,487 patients aged 18 years or older at high cardiovascular risk due to previous cardiovascular events or diabetes mellitus (DM). The mean age of the patients was 67.1 years, and 43.2% were female.</p>	<p>cross-sectional study</p>	<p>69.4% of high-risk patients were receiving lipid-lowering therapy. Of these patients, 47.2% achieved the lipid-lowering therapy goal. Factors associated with achieving the lipid-lowering therapy goal included younger age, higher educational level, lower body mass index, and a higher number of cardiovascular risk factors. Statin therapy was the most commonly used lipid-lowering</p>	<p>Level III, descriptive study</p>	<p>The study was conducted in French general practices and may not be generalizable to other populations</p>	<p>Yes, a substantial proportion of high-risk patients in French general practice are not achieving their lipid-lowering therapy goals. This highlights the need for interventions to improve lipid-lowering therapy adherence and achievement of treatment goals in high-risk patients.</p>



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				agent, and 48.1% of patients receiving statin therapy achieved the lipid-lowering therapy goal.			
<p>Hisni, D., Rukmaini, R., Saryono, S., Chinnawong, T., &amp; Thaniwattananon, P. (2019). Cardiovascular self-management support program for preventing cardiovascular complication behaviors and clinical outcomes in the elderly with poorly controlled type 2 diabetes mellitus in Indonesia: A pilot study. <i>Japan Journal of Nursing Science</i>, 16(1), 25–36.</p>	<p>The purpose of the study was to investigate the feasibility and effectiveness of a cardiovascular self-management support program based on the 5A’s self-management support model in improving the prevention of cardiovascular complication</p>	<p>12 participants, all elderly individuals with poorly controlled type 2 diabetes mellitus. They were randomly assigned to either the experimental group or the control group using a matching technique based on age and sex. The</p>	<p>Quasi-experimental design.</p>	<p>The experimental group showed significantly better clinical outcomes compared to the control group for fasting blood glucose (FBG), total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, systolic blood pressure, and</p>	<p>Level II, quasi-experimental design.</p>	<p>A small sample size (<math>N = 12</math>) and short duration (6 weeks) may limit the generalizability and long-term sustainability of the findings.</p>	<p>Yes, this study can be used as evidence to support the implementation of a cardiovascular self-management support program based on the 5A’s self-management support model for elderly individuals with poorly</p>

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<a href="https://doi.org/10.1111/1/jjns.12208">https://doi.org/10.1111/1/jjns.12208</a>	behaviors and clinical outcomes in elderly individuals with poorly controlled type 2 diabetes mellitus in Indonesia.	mean age of participants in the experimental group was 63.67 (SD = 3.14) years and 62.67 (SD = 4.08) years in the control group. Both groups had similar demographic characteristics, and most of the participants had graduated from senior high school, were housewives, and had experienced diabetes for more than 5 years.		diastolic blood pressure ( $p < .05$ ).			controlled type 2 DM.

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<p>Jun, J. E., Jeong, I. K., Ahn, K. J., Chung, H. Y., &amp; Hwang, Y. C. (2021). Statin use for primary prevention in patients with type 2 diabetes: Can it benefit all ages? – A nationwide propensity-matched cohort study. <i>Diabetes Research and Clinical Practice</i>, 180, Article 109044. <a href="https://doi.org/10.1016/j.diabres.2021.109044">https://doi.org/10.1016/j.diabres.2021.109044</a></p>	<p>The purpose of this study was to investigate the effectiveness of statin use for primary prevention in patients with type 2 diabetes across different age groups.</p>	<p>The cohort included 169,183 patients with type 2 diabetes who were aged between 30 and 75 years, and who did not have a history of CVD. The patients were divided into three age groups: 30-49, 50-64, and 65-75 years.</p>	<p>Retrospective cohort study</p>	<p>Statin use was associated with a significantly lower risk of cardiovascular events in all age groups. The hazard ratios (HRs) for statin users compared to non-users were 0.49 (95% CI [0.42, 0.56] in the 30-49 age group, 0.72 (95% CI [0.67, 0.77] in the 50-64 age group, and 0.87 (95% CI [0.80, 0.95] in the 65-75 age group. The study also found that the risk reduction was greater in patients with higher baseline</p>	<p>Level II, retrospective cohort study with propensity score matching.</p>	<p>Only included patients from Korea, which may limit the generalizability of the findings to other populations.</p>	<p>The study provides evidence that statin use for primary prevention is effective in reducing the risk of cardiovascular events in DM patients, across different age groups.</p>

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				cardiovascular risk.			
<p>Jung, H. H. (2021). Statin use and outcome risks according to predicted CVD risk in Korea: A retrospective cohort study. <i>PLoS One</i>, 16(1), Article e0245609. <a href="https://doi.org/10.1371/journal.pone.0245609">https://doi.org/10.1371/journal.pone.0245609</a></p>	<p>The purpose was to evaluate the association between statin use and CVD outcomes among individuals with varying predicted CVD risk in Korea.</p>	<p>Korean National Health Insurance Service database of 2,333,308 individuals aged 40-79 years, 48.4% men and 51.6% women.</p>	<p>Retrospective cohort study</p>	<p>The study found that statin use was associated with a significantly lower risk of MACE and all-cause mortality among individuals with a predicted 10-year CVD risk of <math>\geq 7.5\%</math>. No significant association between statin use and MACE or all-cause mortality among individuals with a predicted 10-year CVD risk of <math>&lt; 7.5\%</math>.</p>	<p>Level II, retrospective cohort study with a large sample size and control</p>	<p>No information on patient adherence to statin therapy or reasons for statin use.</p>	<p>Yes, the study supports the current guidelines recommending statin therapy for primary prevention in individuals with a 10-year CVD risk of <math>\geq 7.5\%</math></p>
<p>Kamal, A. K., Khalid, W., Muqheet, A., Jamil, A., Farhat,</p>	<p>The purpose was to evaluate the</p>	<p>395 adult stroke and heart attack</p>	<p>RCT</p>	<p>The study found that “talking” prescription</p>	<p>Level II, RCT</p>	<p>Short follow-up period of</p>	<p>Yes, the study supports the</p>

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<p>K., Gillani, S. R. A., Zulfiqar, M., Saif, M., Muhammad, A. A., Zaidi, F., Mustafa, M., Gowani, A., Sharif, S., Bokhari, S. S., Tai, J., Rahman, N., Sultan, F. A. T., Sayani, S., &amp; Virani, S. S. (2018). Making prescriptions “talk” to stroke and heart attack survivors to improve adherence: Results of a randomized clinical trial (the talking rx study). <i>PLoS One</i>, 13(12), Article e0197671. <a href="https://doi.org/10.1371/journal.pone.0197671">https://doi.org/10.1371/journal.pone.0197671</a></p>	<p>effectiveness of a medication adherence intervention using “talking” prescription labels to improve medication adherence and clinical outcomes among stroke and heart attack survivors</p>	<p>survivors who were prescribed at least one medication, 67.1% male, mean age of 61.2 years. Ethnically diverse, with 30.1% identifying as White, 37.2% as Black, and 25.6% as Asian.</p>		<p>labels were associated with a significant improvement in medication adherence compared to standard prescription labels. There was no significant difference in clinical outcomes between the two groups.</p>		<p>only 3 months and the possibility of selection bias in the recruitment of participants.</p>	<p>use of “talking” prescription labels as an effective intervention to improve medication adherence among stroke and heart attack survivors.</p>
<p>Kim, J. Y., Choi, J., Kim, S. G., &amp; Kim, N. H. (2022). Relative</p>	<p>The purpose was to evaluate the contributions</p>	<p>Population-based cohort of 132,849 patients with</p>	<p>Retrospective cohort study</p>	<p>The study found that higher statin intensity, lower achieved LDL</p>	<p>Level II is a population-based</p>	<p>The study is retrospective and observation</p>	<p>They provide valuable insights into</p>

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<p>contributions of statin intensity; achieved low-density lipoprotein cholesterol level, and statin therapy duration to cardiovascular risk reduction in patients with type 2 diabetes: Population-based cohort study. <i>Cardiovascular Diabetology</i>, 21(1), Article 28. <a href="https://doi.org/10.1186/s12933-022-01466-z">https://doi.org/10.1186/s12933-022-01466-z</a></p>	<p>of statin intensity, achieved LDL cholesterol level, and statin therapy duration to CVD risk reduction in patients with type 2 DM</p>	<p>type 2 DM in Korea, mean age of 60.6 years, and 51.8% were male. The mean follow-up period was 4.2 years.</p>		<p>cholesterol level, and longer statin therapy duration lowered the risk of cardiovascular events in patients with DM. Compared to low-intensity statin therapy, high-intensity statin therapy was associated with a lower risk of cardiovascular events (HR 0.80, 95% CI [0.76, 0.84].</p>	<p>cohort study with a large sample size and a long follow-up period.</p>	<p>al, which limits the researchers' ability to draw causal inferences.</p>	<p>the relative contributions of statin intensity and statin therapy duration to cardiovascular risk reduction in DM. The study's findings support the use of high-intensity statins and longer statin therapy duration in these patients to reduce cardiovascular risk.</p>
<p>Kuo, F., Huang, W., Tang, P., Cheng, C., Chiang, C., Lin, H.,</p>	<p>The purpose was to investigate the</p>	<p>1,279 patients with ESRD and AMI, of</p>	<p>Case-control design to</p>	<p>Patients taking statins had a significantly</p>	<p>Level III, case-control</p>	<p>Potential for confounding factors that</p>	<p>Yes, the study supports the</p>

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<p>Chuang, T., Wann, S., Mar, G., Liu, C., Cheng, J., &amp; Wu, M. (2021). Impact of statin on long-term outcome among patients with the end-stage renal disease with acute myocardial infarction (AMI): A nationwide control case-control study. <i>Postgraduate Medical Journal</i>, 97(1147), 299–305. <a href="https://doi.org/10.1136/postgradmedj-2019-137292">https://doi.org/10.1136/postgradmedj-2019-137292</a></p>	<p>impact of statin use on long-term outcomes, including mortality and cardiovascular events, among patients with end-stage renal disease (ESRD) who have experienced acute myocardial infarction (AMI).</p>	<p>which 459 were taking statins and 820 were not. The mean age of the patients was 68 years, and the majority were male (63%).</p>	<p>compare the long-term outcomes of patients with ESRD and AMI who were taking statins to those who were not taking statins.</p>	<p>lower risk of all-cause mortality (adjusted HR 0.63, 95% CI [0.52, 0.77], cardiovascular mortality (adjusted HR 0.57, 95% CI 0.43-0.75), and cardiovascular events (adjusted HR 0.73, 95% CI [0.57, 0.94] compared to those who were not taking statins.</p>	<p>study design.</p>	<p>were not accounted for in the analysis.</p>	<p>use of statins in patients with ESRD and AMI to improve long-term outcomes, including reducing the risk of all-cause mortality, cardiovascular mortality, and cardiovascular events.</p>
<p>Lan, N. S. R., Fegan, P. G., Rankin, J. M., Bell, D. A., Watts, G. F., &amp; Yeap, B. B. (2019). Implementing simple algorithms to improve glucose and lipid management in people with diabetes and acute coronary</p>	<p>The purpose of the study was to evaluate the effectiveness of implementing decision-support algorithms in improving</p>	<p>205 people in two phases. The mean age of the participants was 62.9 years, and three-quarters were men. More than</p>	<p>Prospective observational design.</p>	<p>The implementation of decision-support algorithms was associated with improved inpatient glycemic control, as</p>	<p>Level IV, a prospective observational study without randomization or</p>	<p>Small sample size, relatively short study period, and single-center design, which limits</p>	<p>The results show significant improvements in glycemic control and increased use of cardioprotec</p>

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syndrome. <i>Diabetic Medicine</i> , 36(12), 1643–1651. <a href="https://doi.org/10.1111/dme.14095">https://doi.org/10.1111/dme.14095</a>	glucose and lipid management in people with diabetes and acute coronary syndrome.	90% of the participants had type 2 diabetes.		indicated by a reduction in the incidence of blood glucose levels above 10 mmol/l. There was also an increase in the prescription of SGLT-2 inhibitors and a trend towards increased high-intensity statin prescriptions at discharge. However, the prescription of non-statin lipid-lowering medications did not significantly increase.	control groups	generalizability.	tive therapies, which are essential for reducing cardiovascular risk in this high-risk population.
Lee, Y.-J., Cho, J. Y., You, S. C., Lee, Y.-H., Yun, K. H., Cho, Y.-H., Shin, W.-Y., Im, S. W., Kang, W.	The study aimed to compare the efficacy and safety of a	1,105 patients with type 2 diabetes and ASCVD who were	RCT	Percentage change in LDL cholesterol level was significantly greater in the	Level I, RCT	Relatively short follow-up period of 12 months.	This study provides evidence for the efficacy and safety



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<p>C., Park, Y., Lee, S. Y., Hong, S.-J, Ahn, C.-M., Kim, B.-K., Ko, Y.-G., Choi, D., Hong, M.-K., Jang, Y., &amp; Kim, J. S. (2023). Moderate-intensity statin with ezetimibe vs. high-intensity statin in patients with diabetes and atherosclerotic cardiovascular disease in the RACING trial. <i>European Heart Journal</i>, 44(11), 972–983. <a href="https://doi.org/10.1093/eurheartj/ehac709">https://doi.org/10.1093/eurheartj/ehac709</a></p>	<p>moderate-intensity statin with ezetimibe versus a high-intensity statin in patients with diabetes and ASCVD.</p>	<p>randomized to receive either a moderate-intensity statin with ezetimibe (<math>n = 553</math>) or a high-intensity statin (<math>n = 552</math>). The mean age of the participants was 63.4 years, and 70% were male.</p>		<p>moderate-intensity statin with ezetimibe group compared to the high-intensity statin group (47.5% vs. 38.6%, <math>p &lt; .001</math>). The incidence of cardiovascular events was not significantly different between the two groups. However, the incidence of new-onset diabetes was significantly lower in the moderate-intensity statin with ezetimibe group compared to the high-intensity statin</p>			<p>of a moderate-intensity statin with ezetimibe compared to a high-intensity statin in patients with diabetes and ASCVD.</p>

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				group (3.8% vs. 7.0%, $p = .035$ ).			
<p>Malmborg, M., Schmiegelow, M. D., Gerds, T., Schou, M., Kistorp, C., Torp-Pedersen, C., &amp; Gislason, G. (2021). Compliance in primary prevention with statins and associations with cardiovascular risk and death in a low-risk population with type 2 diabetes mellitus. <i>Journal of the American Heart Association</i>, 10(13), Article e020395. <a href="https://doi.org/10.1161/JAHA.120.020395">https://doi.org/10.1161/JAHA.120.020395</a></p>	<p>The purpose was to evaluate the compliance of primary prevention with statins and its association with cardiovascular risk and death in a low-risk population with type 2 DM.</p>	<p>Danish National Diabetes Register included a cohort of 28,318 patients with type 2 DM who were aged 40-74 years and without prior CVD.</p>	<p>Retrospective cohort study</p>	<p>Patients with type 2 DM who had high adherence to statin therapy had a significantly lower risk of cardiovascular events and death compared to those who did not use statins. Specifically, the high adherence group had a 46% lower risk of CVD and a 54% lower risk of all-cause mortality.</p>	<p>Level III, retrospective cohort study that examines the association between statin compliance and outcomes in patients with type 2 DM.</p>	<p>The study is based on retrospective data and, therefore, is subject to the limitations inherent in this type of study design.</p>	<p>The study provides evidence that high adherence to statin therapy is associated with a lower risk of cardiovascular events and all-cause mortality in patients with type 2 DM.</p>
<p>McGurnaghan, S., Blackbourn, L. A. K., Mocevic, E., Haagen Pantou, U., McCrimmon, R. J., Sattar, N., Wild, S.,</p>	<p>The purpose of the study is to describe the prevalence of major CVD and risk factor</p>	<p>National registry in Scotland, Scottish Care Information-Diabetes,</p>	<p>Retrospective cohort</p>	<p>The study found that among the participants with type 2 diabetes, 32% had prior CVD, and two-</p>	<p>Level II, large retrospective cohort study.</p>	<p>Incomplete data for some risk factors, lack of information</p>	<p>It provides valuable information on the high prevalence of CVD and</p>

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<p>&amp; Colhoun, H. M. (2019). Cardiovascular disease prevalence and risk factor prevalence in type 2 diabetes: A contemporary analysis. <i>Diabetic Medicine</i>, 36(6), 718–725. <a href="https://doi.org/10.1111/dme.13825">https://doi.org/10.1111/dme.13825</a></p>	<p>control in a contemporary population with type 2 diabetes.</p>	<p>linked to hospital admissions. The sample included 248,400 people with type 2 diabetes. The median age of the sample was 67.5 years, and the median diabetes duration was 7.8 years. Among the participants, 32% had prior CVD (35% of men, and 29% of women). The overall median HbA1c was 55 mmol/mol (7.2%),</p>		<p>thirds had two or more risk factors for CVD, such as elevated HbA1c, high blood pressure, high total cholesterol, high body mass index, or current smoking. The use of metformin was common (58%), but other diabetes drugs with cardiovascular benefits were rarely used.</p>		<p>on reasons for insufficient treatment of elevated risk factors, and the use of a wide definition of CVD, which may include conditions with different levels of severity.</p>	<p>the unmet need for risk factor control in people with type 2 diabetes. The findings emphasize the importance of more intensive clinical management, the use of newer diabetes drugs with demonstrated cardiovascular benefits, and the need for tailored approaches to diabetes</p>

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		median SBP was 132 mmHg, median total cholesterol was 4.1 mmol/l, and mean BMI was 32 kg/m <sup>2</sup> .					care to improve cardiovascular outcomes.
Mohan, A., Vadhariya, A., Majd, Z., Esse, T. W., Serna, O., & Abughosh, S. M. (2021). Impact of a motivational interviewing intervention targeting statins on adherence to concurrent hypertension or diabetes medications. <i>Patient Education and Counseling</i> , 104(7), 1756–1764. <a href="https://doi.org/10.1016/j.pec.2020.12.009">https://doi.org/10.1016/j.pec.2020.12.009</a>	The purpose of the study was to investigate the impact of a motivational interviewing intervention, customized for statins, on adherence to concomitantly used antidiabetic and antihypertensive medications in patients with a history of	The sample size for the intervention group receiving MI for statins was 152 patients, and the control group had 304 patients. For the antidiabetic cohort, there were 53 intervention patients and 102 controls,	Retrospective cohort study	The motivational interviewing intervention customized for statins did not significantly improve adherence to antidiabetic or antihypertensive medications during the 6 months post-intervention. The baseline adherence for antihypertensive and antidiabetic	Level III, retrospective cohort study with a small sample size.	The sample size may have been insufficient to detect significant differences in adherence due to a potential ceiling effect in baseline adherence.	The study provides valuable evidence on the impact of a motivational interviewing intervention on medication adherence in patients with multiple chronic conditions. While the

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	suboptimal adherence to statins.	while for the antihypertensive cohort, there were 80 intervention patients and 159 controls.		medications in both intervention and control groups was already above 0.80, suggesting a potential ceiling effect and limited room for improvement in adherence.			intervention did not significantly improve adherence to concomitant antidiabetic and antihypertensive medications, the findings highlight the need for more tailored and individualized interventions to address specific medication adherence barriers.

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<p>Ozen, G., Dell’Aniello, S., Pedro, S., Michaud, K., &amp; Suissa, S. (2023). Reduction of cardiovascular disease and mortality versus risk of new-onset diabetes mellitus with statin use in patients with rheumatoid arthritis. <i>Arthritis Care &amp; Research</i>, 75(3), 597–607. <a href="https://doi.org/10.1002/acr.24866">https://doi.org/10.1002/acr.24866</a></p>	<p>The purpose was to assess the risk-benefit of statin use in patients with rheumatoid arthritis in terms of the reduction of CVD and mortality compared to the risk of new-onset DM.</p>	<p>Quebec health care databases with 21,949 rheumatoid arthritis patients who were newly treated with statins and had no history of CVD or DM. The mean age was 63 years, and 78% were female.</p>	<p>Retrospective cohort study</p>	<p>The study found that statin use was associated with a lower risk of CVD (HR: 0.77, 95% CI [0.65, 0.92] and mortality (HR: 0.71, 95% CI [0.60, 0.84], but a higher risk of new-onset DM (HR: 1.22, 95% CI [1.12, 1.33]).</p>	<p>Level II, retrospective cohort study with a large sample size and control for confounding variables.</p>	<p>Potential for unmeasured confounding, as this was a retrospective study, and the diagnosis of rheumatoid arthritis, CVD, and DM were based on medical codes rather than clinical assessments.</p>	<p>No, study suggests that statin use in patients with rheumatoid arthritis is associated with a reduction in CVD and mortality but an increased risk of new-onset DM.</p>
<p>Panozzo, C. A., Curtis, L. H., Marshall, J., Fine, L., Wells, B. L., Brown, J. S., Haynes, K., Pawloski, P. A., Hernandez, A. F., Malek, S., Syat, B., &amp; Platt, R. (2019). Incidence of statin</p>	<p>The purpose was to assess the incidence of statin use among older adults with and without CVD and DM in the United States from January</p>	<p>45 million beneficiaries were stratified by the presence or absence of CVD and DM, resulting in four groups:</p>	<p>Retrospective cohort study</p>	<p>The highest incidence was in the CVD/DM group, followed by the CVD-only and DM-only groups. The lowest incidence was in the group without CVD or</p>	<p>Level III, Retrospective cohort study</p>	<p>The study relied on claims data to identify individuals with CVD, DM, and statin prescriptions, which</p>	<p>Yes, the study highlights the need for improved prescribing practices for statins in older adults</p>

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
<p>use in older adults with and without cardiovascular disease and diabetes mellitus, January 2008- March 2018. <i>PLoS One</i>, 14(12), Article e0223515. <a href="https://doi.org/10.1371/journal.pone.0223515">https://doi.org/10.1371/journal.pone.0223515</a></p>	<p>2008 to March 2018.</p>	<p>CVD/DM, CVD only, DM only, and neither CVD nor DM. All over 65</p>		<p>DM. Despite the increasing incidence, a significant proportion of individuals with CVD or DM were not prescribed statins.</p>		<p>may have resulted in misclassification.</p>	<p>with CVD and DM.</p>
<p>Rana, J. S., Liu, J. Y., Moffet, H. H., Boklage, S. H., Khan, I., &amp; Karter, A. J. (2018). Risk of incident atherosclerotic cardiovascular disease events by achieved atherogenic lipid levels among 62,428 statin-treated individuals with diabetes mellitus. <i>The American Journal of Cardiology</i>, 122(5), 762–767.</p>	<p>The purpose was to assess the risk of incident ASCVD events in individuals with diabetes who were treated with statins based on their achieved atherogenic lipid levels.</p>	<p>62,428 diabetics who were treated with statins. The sample was 52.8% males and 47.2% females, and the mean age was 62.5 years.</p>	<p>Retrospective cohort study</p>	<p>Individuals with achieved non-HDL cholesterol levels of less than 100 mg/dL had the lowest risk of incident ASCVD events. Individuals with achieved non-HDL cholesterol levels of 100-129 mg/dL had a higher risk of ASCVD events, and individuals with achieved</p>	<p>Level III, a retrospective cohort study.</p>	<p>The study only assessed the risk of ASCVD events and did not assess other outcomes such as medication adherence or cost-effectiveness</p>	<p>This study provides valuable information on the relationship between achieved atherogenic lipid levels and the risk of ASCVD events in individuals with diabetes who are</p>

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
<a href="https://doi.org/10.1016/j.amjcard.2018.05.011">https://doi.org/10.1016/j.amjcard.2018.05.011</a>				non-HDL cholesterol levels of 130 mg/dL or higher had the highest risk of ASCVD events. Similar associations were observed for apoB levels.			treated with statins.
Singh, B. M., Lamichhane, H. K., Srivatsa, S. S., Adhikari, P., Kshetri, B. J., Khatiwada, S., & Shrestha, D. B. (2020). Role of statins in the primary prevention of atherosclerotic cardiovascular disease and mortality in the population with mean cholesterol in the near-optimal to borderline high range: A systematic review and meta-	The purpose was to evaluate the role of statins in the primary prevention of ASCVD and mortality in the population with mean cholesterol in the near-optimal to borderline high range.	11 RCTs with a total of 96,043 participants, predominantly middle-aged (mean age range 49 to 67 years), male (60% to 100%) from different regions, including the United States, Europe, Asia, and Australia.	Systematic review and meta-analysis of RCTs that compared statin therapy with placebo	Statin therapy was associated with a significant reduction in the risk of MACE (RR 0.80, 95% CI [0.75, 0.85]) and all-cause mortality (RR 0.88, 95% CI [0.82, 0.94]) compared to placebo or usual care. There was no significant difference in the risk of adverse	Level I, meta-analysis of RCTs	Trials had different designs, follow-up periods, and baseline characteristics of the participants.	Yes, the findings suggest that initiating statin therapy can reduce the risk of cardiovascular events and mortality.

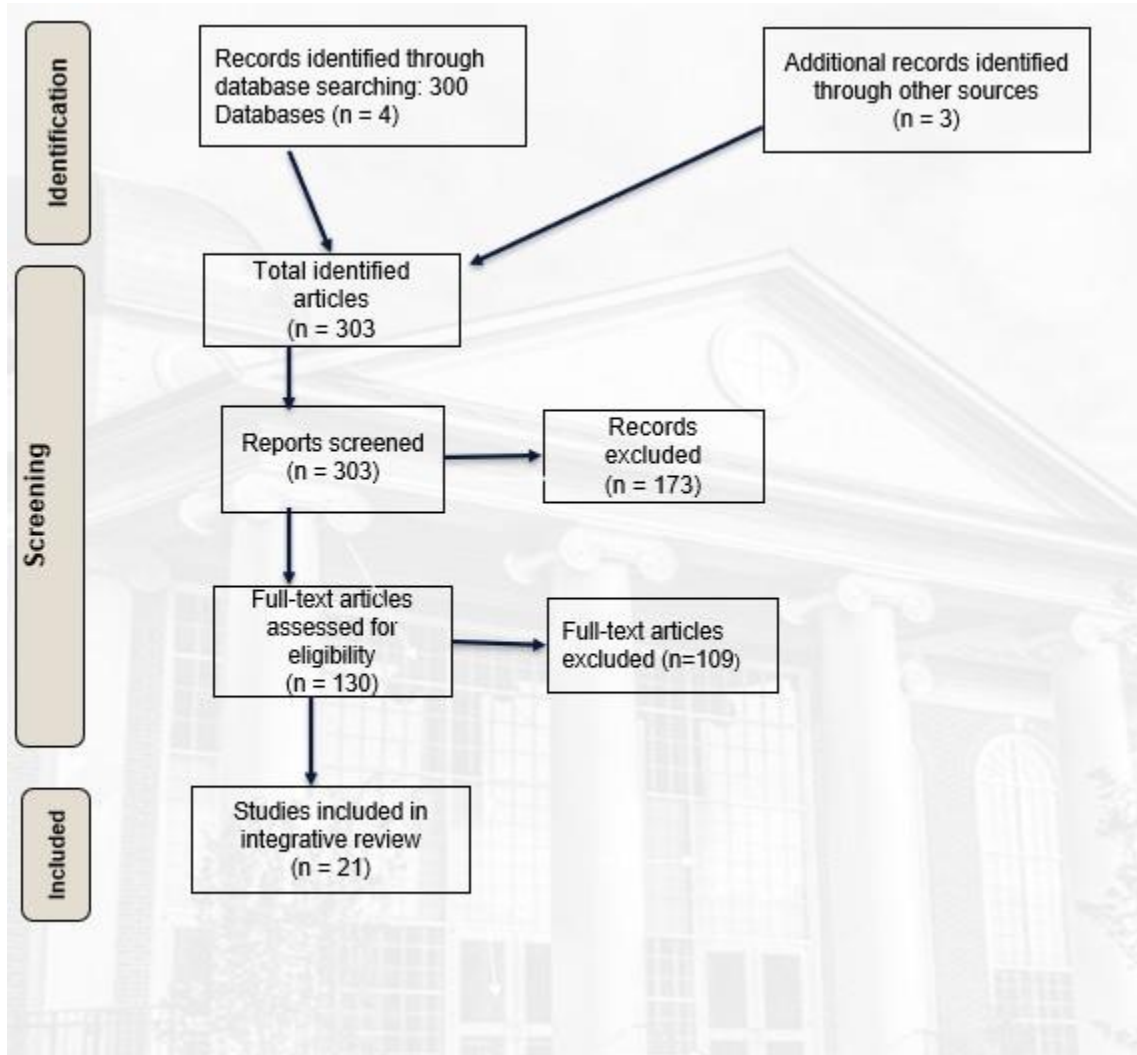


Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
analysis. <i>Advances in Preventive Medicine</i> , 2020, Article 6617905. <a href="https://doi.org/10.1155/2020/6617905">https://doi.org/10.1155/2020/6617905</a>				events between the two groups.			
Tabesh, M., Magliano, D. J., Tanamas, S. K., Surmont, F., Bahendeka, S., Chiang, C.-E., Elgart, J. F., Gagliardino, J. J., Kalra, S., Krishnamoorthy, S., Luk, A., Maegawa, H., Motala, A. A., Pirie, F., Ramachandran, A., Tayeb, K., Vikulova, O., Wong, J., & Shaw, J. E. (2019). Cardiovascular disease management in people with diabetes outside North America and Western Europe in	The study aims to explore changes in anti-hypertensive, lipid-lowering, and antiplatelet medications, as well as in blood pressure (BP) and cholesterol target achievement in people with diabetes outside North America and Western Europe from 2006 to 2015.	39,684 people with type 2 diabetes from eight clinical sites in seven different countries: Argentina, Australia, Hong Kong, India, Japan, Saudi Arabia, and South Africa. Age ranged from 18 to 73 years, and the study population received specialist care services	Retrospective	Statins decreased cholesterol levels significantly in seven out of the eight studies used. The proportion of individuals using antiplatelet medications was generally below 50%, and changes in usage varied across sites.	Level IV, retrospective study with a large sample size but no control group.	The small number of clinical services involved may limit the generalizability of the findings to other settings and resource-limited areas.	The findings align with established evidence that statin therapy is effective in reducing cardiovascular risk in diabetic patients. I would use this information to support the importance of statin therapy in managing

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
2006 and 2015. <i>Diabetic Medicine</i> , 36(7), 878–887. <a href="https://doi.org/10.1111/dme.13858">https://doi.org/10.1111/dme.13858</a>		except in Argentina, where some were treated in primary care.					cholesterol levels in individuals with Type 2 diabetes, emphasizing its role in reducing cardiovascular risk.
Wierzbicki, A. S. (2018). Further options for treating lipids in people with diabetes: Targeting LDL-cholesterol and beyond. <i>Diabetic Medicine</i> , 35(9), 1173–1180. <a href="https://doi.org/10.1111/dme.13667">https://doi.org/10.1111/dme.13667</a>	The purpose of the study was to review and critically evaluate various lipid-lowering interventions, particularly focusing on LDL-cholesterol and other related factors, in the management of individuals with diabetes.	A review of clinical trials.	Systemic review	The article highlights the efficacy of statins, ezetimibe, and PCSK-9 inhibitors in lowering LDL-cholesterol levels and reducing cardiovascular risk in people with diabetes.	Level II, systemic review of clinical trials	The article relied on existing data and any limitations on those studies could apply to the current study.	Yes, the article supports the use of statins, ezetimibe, and PCSK-9 inhibitors for effective LDL-cholesterol reduction and cardiovascular risk reduction.

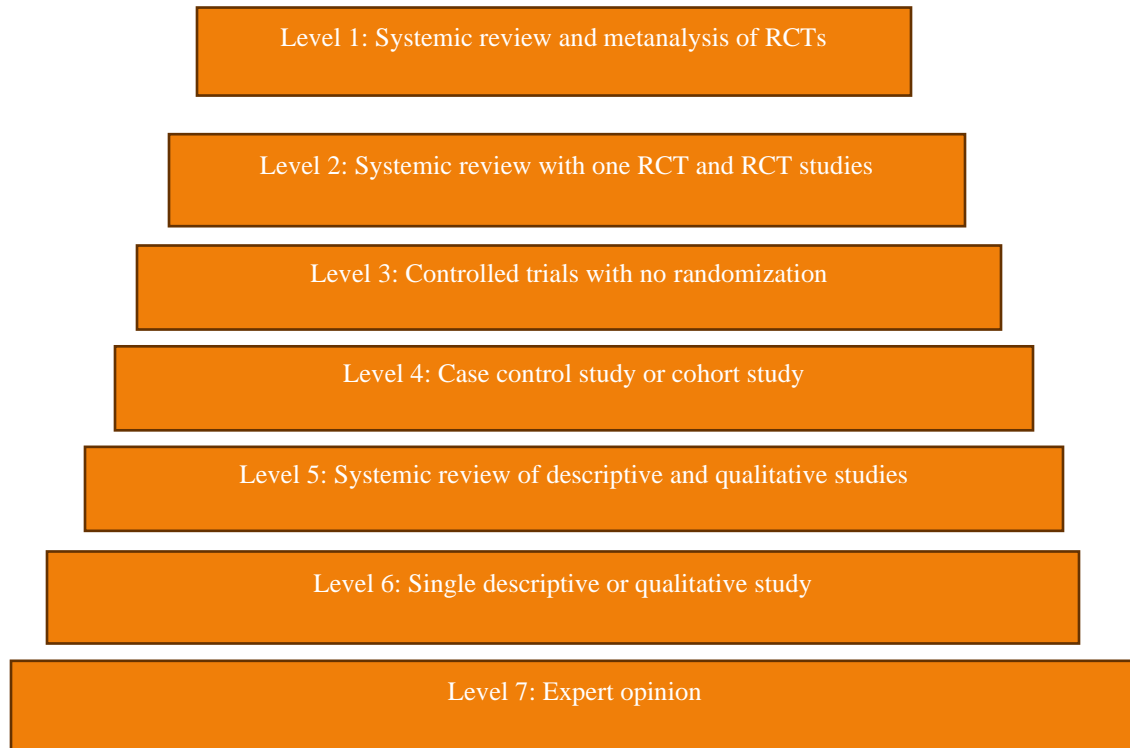
### Appendix B

#### PRISMA 2020 Flow Diagram



## Appendix C

### Melnyk Levels of Evidence



Modified from the Melnyk, B. M., & Fineout-Overholt, E. (2015). *Evidence-based practice in nursing & healthcare: A guide to best practice* (3rd ed.). Wolters Kluwer Health.

## Appendix D

### PRISMA Checklist

Section	What to check
<b>Title</b>	Does the title indicate that the paper is a systematic review or meta-analysis?  Is the title informative, including details about the specific research question or topic?
<b>Abstract</b>	Structured summary of the study, including objectives, methods, results, and conclusions? Does it describe the study type and outline key components?
<b>Introduction</b>	Introduction clearly states the research question, objective, or hypothesis of the study?  Does it explain the importance and rationale for conducting a systematic review or meta-analysis on the topic?
<b>Methods</b>	Does the paper describe the detailed methods used for the systematic review or meta-analysis, including the search strategy, inclusion and exclusion criteria, and data extraction?  Are the methods outlined in a way that allows for reproducibility by others?
<b>Results</b>	Are the results presented in a structured manner, including a flow diagram showing the study selection process?  Does the results section show characteristics of included studies, a summary of findings, and quantitative synthesis?
<b>Discussion</b>	Does the discussion interpret the results in the context of the research question and study objectives? Are the limitations of the study acknowledged, and their potential impact on the findings discussed? Are implications for practice, policy, and future research clearly stated?

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<b>Conclusion</b>	Does the conclusion summarize the main findings of the systematic review or meta-analysis?
<b>Funding</b>	Is information about the funding source and any potential conflicts of interest disclosed?

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Adapted from “Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement,” by D. Moher, A. Liberati, J. Tetzlaff, D. G. Altman, and The PRISMA Group, 2009, *PLoS Med* 6(7), Article e1000097 (<https://doi.org/10.1371/journal.pmed1000097>)

## Appendix E



### Project Completion Timeline

Milestone	Deliverable	Description	Estimated completion
Met	Successfully completed	Dissertation topic submission	January 29, 2023
Met	Successfully completed	Dissertation chair request	January 29, 2023
Met	Successfully completed	Dissertation topic chair approval	February 6, 2023
Met	Successfully completed	CITI training completion	May 16, 2023
Met	Successfully completed	Literature matrix	May 28, 2023
Met	Successfully completed	Proposal defense	June 09, 2023
Met	Successfully completed	Sections I-III	June 30, 2023
Met	Successfully completed	IRB application	June 20, 2023
Met	Successfully completed	IRB approval	June 20, 2023
Met	Successfully completed	Editing and completion of Sections 1–3	July 3, 2023
Met	Successfully completed	Development of Sections 1–5	July 28, 2023
Met	Successfully completed	Completion of manuscripts with appendices for chair review	August 18, 2023
Met	Successfully completed	Editor submission of final manuscripts	September 12, 2023
Met		Final oral defense	October 05, 2023
		Chair approval	After successful defense
		Integrative review submission to Scholars Crossing	After chair approval
		Advancement of the integrative review implementation at the doctor's office	After chair approval

*Note.* CITI = Collaborative Institutional Training Initiative; IRB = Institutional Review Board.

**Appendix F**

**Collaborative Institutional Training Initiative Certificate**



Completion Date 29-Mar-2023  
Expiration Date 29-Mar-2026  
Record ID 55152413

This is to certify that:

**Simone Anckle**


Has completed the following CITI Program course:

**Biomedical Research - Basic/Refresher**  
(Curriculum Group)  
**Biomedical & Health Science Researchers**  
(Course Learner Group)  
**1 - Basic Course**  
(Stage)

Under requirements set by:

**Liberty University**

Not valid for renewal of certification through CME.



Collaborative Institutional Training Initiative  
101 NE 3rd Avenue, Suite 320  
Fort Lauderdale, FL 33301 US  
[www.citiprogram.org](http://www.citiprogram.org)

Verify at [www.citiprogram.org/verify/?wd9a9d834-93cc-449a-aad9-2ffb16b90f01-55152413](http://www.citiprogram.org/verify/?wd9a9d834-93cc-449a-aad9-2ffb16b90f01-55152413)



## APPENDIX G

I

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**LIBERTY UNIVERSITY.**  
INSTITUTIONAL REVIEW BOARD

June 20, 2023

Simone Anckle  
Simone Anckle

Re: IRB Application - IRB-FY22-23-1778 "The Efficacy of statin therapy in reducing cardiovascular accident stroke (CVA) Risk among Type 2 diabetes adults patients using patient-centered Care: An Integrative Review"

Dear Simone Anckle and Simone Anckle,

The Liberty University Institutional Review Board (IRB) has reviewed your application in accordance with the Office for Human Research Protections (OHRP) and Food and Drug Administration (FDA) regulations and finds that your study does not meet the definition of human subjects research. This means you may begin your project with the data safeguarding methods mentioned in your IRB application.

Decision: No Human Subjects Research

Explanation: Your project is not considered human subjects research because it will not involve the collection of identifiable, private information from or about living individuals (45 CFR 46.102). Please note that this decision only applies to your current application. Any modifications to your protocol must be reported to the Liberty University IRB for verification of continued non-human subjects research status. You may report these changes by completing a modification submission through your Cayuse IRB account.

If you have any questions about this determination or need assistance in determining whether possible modifications to your protocol would change your application's status, please email us at [irb@liberty.edu](mailto:irb@liberty.edu).

Sincerely,

**G. Michele Baker, PhD, CIP**  
*Administrative Chair*  
**Research Ethics Office**

**APPENDIX H**

**List of Tables**

Table 1. Inclusion and Exclusion Criteria.....30