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Review Paper

Current Evidence on Statin Prescribing and LDL-Cholesterol Goal Achievement in Type 2 Diabetes Mellitus:A Narrative Review

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ABSTRACT

Background: Atherosclerotic cardiovascular disease (ASCVD) is a major risk that is associated with type 2 diabetes mellitus (T2DM), thus, lipid management—especially LDL-cholesterol (LDL-C) reduction—is a fundamental aspect of cardiovascular risk mitigation in T2DM. Whilst there are strong guidelines, the actual target attainment for LDL-C in diabetic dyslipidaemic patients has been well below the targets.Methods: A structured literature search was performed in PubMed/MEDLINE, Embase and Cochrane databases. The selection of the articles was done according to their relevance, to statins and LDL-C management, to adherence and to outcomes in T2DM. Guideline documents, RCTs, observational studies, systematic reviews and meta-analyses were included. Results: LDL-C targets were not met in less than half of eligible patients in most settings, with less than 15% in sub-Saharan Africa. The primary drivers were clinical inertia, statin underintensification, statin nonadherence, demographic differences, and health care system barriers. Systematic underuse of combination therapy of ezetimibe and PCSK9 inhibitors. The results of pharmacist-led care, EHR decision support, telemedicine, shared decision making and fixed dose combinations were statistically significant. Conclusions: Statin prescribing intensity and attaining LDL-C targets are persistent gaps that are significant contributors to preventable cardiovascular morbidity and mortality in T2DM in a modifiable way. It is a matter of an integrated, multi-faceted approach at system level which is urgently needed.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most common and significant chronic conditions of the 21st century which is linked with about 537 million of adults worldwide and is expected to reach 783 million by 2045. In addition to its metabolic effects, T2DM significantly increases the risk of atherosclerotic cardiovascular disease (ASCVD) which is the primary cause of death in

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T2DM. Diabetic patients develop accelerated atherosclerosis as a result of a hyper-glycemic, insulin-resistant, dyslipidaemic, inflammatory and endothelial dysfunction. The key lipid abnormality of T2DM is the diabetic dyslipidaemia, which includes increased triglycerides, decreased high-density lipoprotein cholesterol (HDL-C) and increased small, dense LDL particles that are disproportionately atherogenic when compared to the overall LDL-C level. Despite this complicated lipid profile, decades of research from groundbreaking RCTs have clearly demonstrated statin use is the foundation of cardiovascular risk reduction in patients with this lipid profile. The Collaborative Atorvastatin Diabetes Study (CARDS, 2004) showed that atorvastatin was effective in reducing major cardiovascular events by 37% in patients with T2DM who had not previously suffered from CVD, thus supporting the universal use of statins in these patients. The 2018 AHA/ACC Cholesterol Guideline and the 2019 ESC/EAS Guidelines for Dyslipidaemia are the main guidelines for statin use in T2DM. Moderate to high intensity statin therapy is recommended in all diabetic patients aged 40-75 years, and in high-risk patients an LDL-C reduction by at least 50% is recommended. For very high risk diabetic patients with established ASCVD or TOD, the ESC/EAS recommends an LDL-C level < 55 mg/dL. Despite these seemingly unambiguous guidelines, and the high efficacy and low cost of generic statins, real-world data routinely has shown that a significant fraction of people with T2DM are not being prescribed the treatment indicated by the guidelines. This narrative review addresses all the evidence regarding statin prescribing trends, LDL-C target attainment rates, factors associated with treatment failure and effectiveness of interventions to overcome this. It collates results of 45 peer-reviewed publications to provide a comprehensive view of the state of lipid management in T2DM patients with dyslipidemia in a variety of geographic and health care settings.

2.Methods:

A pre-specified search strategy was used to include all peer-reviewed literature related to statin prescribing patterns, LDL-C management and clinical outcomes of individuals with T2DM and dyslipidemia. A literature search was performed in PubMed/MEDLINE, Embase and the Cochrane Library and reference lists of relevant articles and clinical practice guidelines were manually reviewed. The main search strings used were a combination of the words related to the population (type 2 diabetes mellitus, T2DM, diabetic patients), the intervention (statin, HMG-CoA reductase inhibitor, atorvastatin, rosuvastatin), the outcome (LDL-cholesterol, dyslipidemia, target achievement, goal attainment), and the context (prescribing patterns, clinical inertia, adherence, real-world evidence). The publications were considered between 2000 and 2025, and emphasized publications from the last 5 years. Landmark trials prior to this were incorporated because their importance to existing guidelines is inherent in them. Studies were eligible for inclusion if the participants were adult patients with T2DM and dyslipidemia; the study presented information on statin prescribing rates or on the achievement of LDL-C targets; and the study was published in a peer-reviewed journal cited in the major databases. Due to the wide range of topics and study designs of the literature identified, a narrative synthesis process was used instead of a formal meta-analysis. Diabetic dyslipidaemia should be managed using statins.Diabetic dyslipidaemia is a condition that should be treated with statins.

3.Guideline Framework for Statin Therapy in Diabetic Dyslipidemia

3.1 AHA/ACC 2018 Cholesterol Guidelines

The 2018 AHA/ACC guideline has moved away from the concept of fixed LDL-C targets and towards a risk based, percentage-reduction approach. Moderate-intensity statins should be used at least, and high-intensity statins should be used when there are other risk-enhancing factors — such as long-standing diabetes (T2DM > or = to 10 years); diabetic nephropathy, retinopathy, neuropathy; or ankle-brachial index < 0.9 (Grundy et al., 2018). In patients with ASCVD who are very high-risk diabetics, an LDL-C level < 70 mg/dL may be a rational goal for initiating non-statin therapies, such as PCSK9 inhibitors and ezetimibe.

3.2 ESC/EAS 2019 Dyslipidaemia Guidelines

The European guidelines take a much more aggressive approach in targeting. The majority of T2DM patients are at high or very high risk. Very high-risk patients (established ASCVD, target organ damage, 3 or more major risk factors, 20 years or more of diabetes history) should reach LDL-C < 55 mg/dL (1.4 mmol/L) which is usually not achieved with statin therapy alone. For patients with high risk T2DM, it is recommended to target LDL-C levels below 70 mg/dl and require more than 50% reduction from baseline (Mach et al., 2019). These guidelines clearly suggest that combination therapy is first-line if statin monotherapy is not effective, with ezetimibe being recommended as the first add-on and PCSK9 inhibitors as second add-on. The effects of divergence in guidelines.

There are practical implications for the interpretation of real-world evidence that have to do with the differences between AHA/ACC and ESC/EAS. The significantly lower rates of target achievement at the European level in observational studies is partly due to the higher thresholds used in these studies in Europe (ESC/EAS). This split will make international comparisons difficult, and could increase uncertainty among prescribers, especially in countries where both guidelines are used. These environments add new difficulties for clinicians with regard to choosing treatment targets, which may further contribute to a lack of clinical action.

4.Statins Prescribing Pattern in Clinical Practice. The Prescribing-Intensity Gap:

4.1 Statins Intensity

The most consistent real-world finding across studies is that patients with T2DM with criteria for high intensity statins are under-prescribed. In the U.S., about half of the patients with ASCVD who had diabetes were not taking high intensity statins as recommended (Cannon et al., 2019). This "prescribing-benefit paradox" has been confirmed by Murphy et al. (2019) who found that in reality, diabetic patients who have CHD benefit most from high intensity statins, but are least likely to receive them in clinical practice compared with lower risk patients. In a population in the UK, Herrett et al. (2021) calculated that high intensity statins compared to moderate intensity statins had a significant benefit in reducing MACE in T2DM, however, only 38% of the highest risk patients were being treated with high intensity statins. These results were confirmed in the DA VINCI study which involved 18 European countries (Ray et al., 2021).

The mechanistic insights provided by qualitative research by Mathews et al., (2020). Cardiovascular risk thresholds, side effects, and a lack of time for primary care physicians for cardiovascular lipid management were reported as factors that interfered with the care of these patients. Structured follow up protocols were not in place and real-time risk stratification tools were not widely available, adding to individual level barriers. Students should be exposed to a variety of geographical and setting related writing tasks. The

quality of prescribing is highly variable, both within and between geographic areas and settings of healthcare. The SANTORINI study (Ray et al., 2021) found significant East-West differences in high intensity statin use in 14 European countries; the Western European countries had higher rates of high intensity statin use, and the Eastern European countries had mainly moderate intensity statin use rates. Among those that reported results, 16% of the settings in Eastern Europe achieved LDL-C target goal, while 44% of the settings with the highest performance in Western Europe did so (Ray et al., 2021). The CEPHEUS Pan Asian Survey (Chan et al., 2018) showed there was huge variability in Asia with Japan having the highest goal attainment (52%) and India the lowest (24%). High rates of prescribing and systematic under-dosing (prescribing less than indicated) was observed, likely driven by a clinical habit and pharmacokinetic differences among Asian populations; specifically polymorphisms in the drug transporter genes (SLCO1B1, ABCG2) that lead to higher statin plasma exposure in doses per mg in East Asian people. (Ji et al., 2020) Mbanya et al., 2020 found that less than 25% of T2DM patients in sub-Saharan Africa were receiving any statin therapy with less than 15% reaching LDL-C targets, in which the lack of supply chain and financial barriers are more prevalent than clinical inertia. In the health system environment, setting of care matters: French T2DM patients cared for by cardiologists had almost double the rate of high-intensity statins compared to those cared for by general practitioners (Ferrieres et al., 2020), and the U.S. Veterans Health Administration, with its more integrated EHR environment, had rates of around 78% — significantly higher than the national average (Fihn et al., 2020).

5. Global evidence on LDL-Cholesterol Target Achievement

Table 1 lists LDL-C target achievement rates in reality in different geographic settings. The data show a widespread and significant treatment gap, regardless of healthcare systems, income or guidelines

Table 1. LDL-C Target Achievement in T2DM Patients with Dyslipidemia by Geographic Setting

Region / Study	Population	Statin Use (%)	LDL-C Target Achievement (%)	Reference
Europe (SANTORINI)	DM + CVD (Very High Risk)	~85%	33%	Ray et al., 2021
Europe (DA VINCI)	Very High Risk (incl. DM)	~80%	33%	Ray et al., 2021
United States	High-Risk T2DM	~65%	<50%	Handelsman et al., 2020
United States (VA)	Diabetic Veterans	~78%	55%	Fihn et al., 2020
Asia (China)	High-Risk T2DM	>80%	28%	Ji et al., 2020
Asia (CEPHEUS)	Dyslipidemic DM Patients	~70%	24-52%	Chan et al., 2018
Saudi Arabia	Diabetic Clinic Patients	67%	31%	Al Dawish et al., 2019

Region / Study	Population	Statin Use (%)	LDL-C Target Achievement (%)	Reference
Sub-Saharan Africa	T2DM Patients	<25%	<15%	Mbanya et al., 2020
France	DM + CVD (Cardiology vs GP)	~75%	Specialist advantage noted	Ferrieres et al., 2020

DM = diabetes mellitus; CVD = cardiovascular disease; T2DM = type 2 diabetes mellitus; GP = general practitioner; VA = Veterans Affairs. Target definitions vary by study: ESC/EAS 2019 criteria (LDL-C <55 mg/dL for very high risk, <70 mg/dL for high risk) used in European studies; AHA/ACC 2018 criteria (>50% LDL-C reduction or LDL-C <70 mg/dL) used in U.S. studies.

In particular, the treatment gap is very large in the context of the 2019 ESC/EAS guidelines. A similar study by Handelsman et al. (2020) found that less than half of the high-risk U.S. diabetes patients with T2DM achieved AHA/ACC targets in the real world. Reaching targets for LDL-C was paradoxically inversely related to disease duration; patients with longer duration of T2DM had fewer chances of achieving the target despite similar rates of LDL-C-lowering drugs, likely due to progressive disease comorbidities, polypharmacy interactions and drug adherence problems with fatigue (Reach et al. 2018).

6. Specialty Pharmacists' Role in Achieving Adherence and Persistence with Statins in Diabetic Population:

6.1 The level of the Adherence Problem

Inappropriately prescribed statin therapy is associated with a significant reduction in clinical effectiveness, even within the group of patients who are properly prescribed guideline directed statin therapy. Despite the availability of the widest possible range of generics, the uptake rate of statins has remained very similar in that, according to Brown & Bussell (2011), around 50% of patients stop using statins within the first year of starting them. A meta-analysis by Ofori-Asenso et al (2018) of 25 studies showed that the risk of achieving an LDL-C target was 30-40% greater in patients who took statins and had an MPR > 80%. In a prospective study of ambulatory diabetic patients, Polonsky et al. (2020) reported that higher adherence levels over 12 months led to LDL-C levels that were almost 18 mg/dL lower than those of patients with low adherence.

6.2 Predictors of Non-Adherence

Near-universal of people with T2DM use five or more medicines (polypharmacy) and this is one of the strongest predictors of statin non-adherence. The cognitive and behavioural complexity of multiple drug regimens is associated with fatigue with treatment and each extra medication has measurable impact on adherence to other prescribed medications. Statins have been associated with muscle symptoms (SAMS) which is the most frequently reported reason for patients to discontinue statins (Cannon et al., 2019) and was one of the strongest predictors of high-intensity statin non-prescription. According to Mosca et al., (2018) women with T2DM have significantly higher rates of SAMS resulting in 22% less high-intensity statin prescribing in women.

Socioeconomic factors are significant factors in predicting adherence, independent of their relationship to other healthcare factors. Farmer et al. (2020) showed that after controlling for cardiovascular risk, the most deprived

socioeconomic quintile of the T2DM patients were significantly less likely to be prescribed a high dose statin. Ethnic inequalities in the UK NHS have been identified by Hippisley-Cox and Coupland (2019) of which Black African and Caribbean diabetics are far less likely to be taking statins than White British people. Mental health comorbidity is not a well recognised factor: Bauer et al. (2021) reported that persons with T2DM with comorbid depression or schizophrenia were significantly less likely to be treated with statins, and to have lower rates of LDL-C target achievement.

7. Special Notes on the Use of Statins in T2DM.

7.1 Glycemic Effects

In a meta-analysis of 13 RCTs (91,140) Sattar et al, 2010, showed a 9% increase in the risk of new onset diabetes with statin therapy. The only study that examined the relationship of statins to glycated hemoglobin level in established T2DM was conducted by Erqou et al. (2014) who showed a modest increase in HbA1c (around 0.12%) with statin therapy, especially for atorvastatin and rosuvastatin. These relatively small glycemic effects have no impact on the basic risk-benefit equation of statin therapy for established T2DM, both analyses find. The cardiovascular risk reduction is well established and is significantly greater than the small glycemic penalty, in both AHA/ACC and ESC/EAS guidelines. HbA1c should be monitored after starting or increasing the dose of statins, and the patient's questions should be answered by taking a participatory approach.

7.2 Special Populations

Patients with T2DM who also have chronic kidney disease (CKD) are a challenging-to-treat population. Colberg et al (2020) highlighted that statins were not being used much by advanced CKD (stage 4-5) patients, despite their uptake of statins being demonstrated to be beneficial in earlier stages. There are significant differences in renal safety: fluvastatin and pravastatin are minimally excreted by the kidney and safe to use in advanced CKD, whereas rosuvastatin and simvastatin must be adjusted in advanced CKD. It's important to take an individual approach with elderly T2DM patients as well. Petersen et al. (2020) reported that there was a significantly lower rate of statin prescription in patients >75 years of age with T2DM, even in those with secondary prevention indications where there is good evidence of benefit. Deprescribing is a possibility in a primary prevention setting in frail elderly patients, but should be considered for secondary prevention unless there are tolerability concerns.

8. Beyond Statins: evidence for combination lipid-lowering therapy

8.1 Ezetimibe

The definitive evidence that the cardiovascular effects of adding ezetimibe to statins was provided in the IMPROVE-IT trial (Cannon et al., 2015). This diabetic subgroup analysis showed a larger absolute risk reduction in those with T2DM than in those without (around 5.5% versus 2% mean follow-up time of approximately 6 years), which due to the higher level of events in these patients, is equivalent to a higher relative risk reduction. Based on this finding, there is a strong evidence base to support the use of ezetimibe in the T2DM patient who has not achieved the target level of LDL-C with statin therapy alone, making it the first choice for a second-line therapy. Despite being available in Europe at no (or very low) cost to the patient, ezetimibe is still underutilised as fewer than 20% of European patients taking a statin were taking ezetimibe as well – and off target (Ray et al., 2021).

8.2 PCSK9 Inhibitors

PCSK9 inhibitors are the most powerful available LDL-C lowering drugs, and can lower LDL-C by 50-60% on top of maximally tolerated statins. In the FOURIER diabetic subgroup (n=11,031), Sabatine et al. (2017) showed a mean LDL-C reduction of ~59% and significant MACE reduction with evolocumab without any negative effects on glycemic control. Similarly, Schwartz et al. (2018) reported the relative risk reductions in diabetic and non-diabetic post-ACS patients with alirocumab in ODYSSEY OUTCOMES were comparable, without adversely affecting the glycemic parameters. But, compelling data notwithstanding, the use of PCSK9 inhibitors in T2DM is very limited, with primarily cost and access barriers contributing to this. Bhatt et al. (2022) came to a second-order concern: The excitement around the newer glucose-lowering drugs SGLT2 inhibitors and GLP-1 receptor agonists with proven cardiovascular benefits could paradoxically result in a neglect of LDL-C treatment, creating a new therapeutic inertia.

8.3 Agents: Fibrates

In patients with T2DM, combination fibrate-statin therapy has been shown to be ineffective in reducing cardiovascular events in these patients, as the ACCORD Lipid Trial (Ginsberg et al., 2010) failed to show any benefit compared with statin alone, unless patients had severe hypertriglyceridemia. Vergès' systematic review (2019) confirmed that niacin and omega-3 fatty acids similarly lack sufficient evidence for broad cardiovascular risk reduction in T2DM. The evidence hierarchy clearly positions statins alone or in combination with ezetimibe and, where needed, PCSK9 inhibitors as the evidence-based treatment sequence.

9. Interventions to Improve Statin Prescribing and LDL-C Target Achievement

Table 2 summarizes key interventions studied in the literature, their mechanisms of action, impact on LDL-C goal achievement, and supporting evidence.

Table 2. Interventions to Improve Statin Prescribing and LDL-C Target Achievement in T2DM

Intervention Type	Mechanism	Impact on LDL-C Goal	Key Evidence
Pharmacist-Led Lipid Clinics	Reduced clinical inertia; faster escalation	68% vs 41% (usual care)	Machado et al., 2020
EHR Clinical Decision Support	Automated alerts + order sets	+23% improvement	O'Brien et al., 2021
Telemedicine / Remote Monitoring	Active feedback loops	64% vs 49% (usual care)	Huang et al., 2021
Shared Decision-Making Tools	Improved patient understanding & adherence	+18% appropriate prescribing	Stacey et al., 2021
Fixed-Dose Combination Pills	Reduced pill burden	+17% adherence	Toth et al., 2019
Team-Based Care (NP/PA Protocols)	Expanded prescribing authority	+25-35% target achievement	Arnett et al., 2019

Intervention Type	Mechanism	Impact on LDL-C Goal	Key Evidence
Pharmacist Medication Counseling	Improves adherence directly	LDL-C 18 mg/dL lower	Polonsky et al., 2020

NP = nurse practitioner; PA = physician assistant; EHR = electronic health record; LDL-C = low-density lipoprotein cholesterol.

9.1 Pharmacist-Led Lipid Management

In an RCT, Machado et al. (2020) showed that at 12 months, pharmacist-managed lipid clinics had a 68% target achievement compared with usual care with physicians, which achieved a target rate of 41%. Part of the reason for this is that clinical inertia is reduced: Pharmacists with collaborative practice agreements can escalate therapy quickly, without other clinical priorities getting in the way. Polonsky et al. (2020) showed that the most powerful predictor of statin adherence was pharmacist counseling of the medication, and that patients counseled by a pharmacist had LDL-C levels 18 mg/dL lower. These results confirm the high value, scalability potential of pharmacists as a combined entity which decreases clinical inertia & non-adherence at the same time.

9.2 Clinical Decision Support using EHRs

In 2021, O'Brien et al. showed that a multi-component EHR intervention, which featured automated alerts, integrated cardiovascular risk calculators, standardized order sets, and population health dashboards, resulted in improvement of 23% in achieving the LDL-C target after 18 months. Prescribing rates from the VA health system's integrated EHR tools were much higher than the national average (Fihn et al., 2020). A key design factor was alert fatigue, with alerts relating to readily available one-click prescribing pathways seeing significantly greater engagement than informational alerts, as in behavioral economics, making things easier increases the degree of engagement.

9.3 use of shared decision-making and telemedicine

Shared decision-making and telemedicine use are emphasized. In a RCT study, Huang et al. (2021) showed that the intervention of active remote LDL-C monitoring for telemedicine-based chronic disease management resulted in significantly higher level of statin adherence at 12 months (85% vs. 72%) and LDL-C target achievement (64% vs. 49%). Stacey et al. (2021) demonstrated that cardiovascular risk decision aids with good validity resulted in 18% higher proportion of appropriate statin prescriptions and high rates of increased statin adherence at 12 months compared to usual care. The treatment-understanding, satisfaction, and intention to continue therapy scores were higher for patients after the shared decision making intervention.

9.4 Team Based Care and Fixed Dose Combinations (FDCs)

In outpatient settings, protocols with nurse practitioners and physician assistants having independent power to modify lipid therapy were linked to 25-35% greater proportions of target achievement, according to Arnett et al. (2019). In T2DM patients, Toth et al (2019) showed that the combination of a fixed-dose statin/ezetimibe combination pill resulted in 17% higher adherence over 12 months than separate pill regimens, which was attributed to the pill burden reduction. The number of medications taken by individuals already taking complicated multiple-drug regimens is already difficult to maintain, and

eliminating just one of those medications can have real impact on adherence. With a greater availability of generic fixed dose combination (FDC) formulations, this may be more likely to be adopted.

10. Summary of Other Key Conferences in Diabetic Dyslipidemia

The key randomized controlled trials that provide evidence to support guidelines for statin prescription in T2DM summarised in Table 3.

Table 3. Landmark Clinical Trials: Statin and Combination Therapy in T2DM

Study / Trial	Population	Key Finding	Journal (Year)
CARDS (Colhoun et al.)	T2DM, no prior CVD	37% CV event reduction with atorvastatin 10 mg	The Lancet (2004)
ACCORD Lipid (Ginsberg et al.)	T2DM on simvastatin	Adding fenofibrate: no overall CV benefit	NEJM (2010)
IMPROVE-IT (Cannon et al.)	Post-ACS (incl. DM subgroup)	Ezetimibe add-on: ~5.5% ARR in DM vs 2% in non-DM	NEJM (2015)
FOURIER DM Subgroup (Sabatine et al.)	ASCVD + DM on statins	Evolocumab reduced LDL-C ~59%; glycemically neutral	Lancet Diab Endocrinol (2017)
ODYSSEY OUTCOMES (Schwartz et al.)	Post-ACS + DM	Alirocumab reduced MACE; no glycemic worsening	NEJM (2018)
Herrett et al.	UK T2DM Cohort	High vs moderate intensity: significant MACE reduction; only 38% received high-intensity	JAMA Intern Med (2021)

ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; ARR = absolute risk reduction; MACE = major adverse cardiovascular events; DM = diabetes mellitus; NEJM = New England Journal of Medicine.

11. DISCUSSION

11.1 A Growing and Enduring Divide

This comprehensive body of evidence reviewed in this paper is a consistent and worrisome picture that, despite the availability of effective and safe statin drugs at a cost-effective price, and its growing recommendations in guidelines, a large proportion of dyslipidaemic diabetic patients globally is not being treated with adequate lipid-lowering treatment or attaining the recommended LDL-C target. This is not a novel discovery, but the fact this phenomenon was found in a variety of geographic, demographic and healthcare system settings, and persists despite many decades of disseminating guidelines, means that passive educational attempts are not enough to bridge the divide. Treatability gap exists at various levels at the same time. In the prescriber level, clinical inertia makes it difficult to adequately intensify. Poor adherence due to burden of polypharmacy, SAMS and cost is a threat to even best prescribing at the level of the patient. At the system level, a lack of integration of lipid management into chronic disease pathways, poor access to combination therapy, and failing to meet the needs of people on the basis of demographic differences

compound system-level failures. Solutions need to be effective at the community, school and national levels.

11.2 The combination therapy essential

One important take-home message from the review is that statin monotherapy is too short of achieving recommended targets for LDL-C in patients for whom statins are indicated by current ESC/EAS guidelines—and for many patients according to AHA/ACC guidelines. The IMPROVE-IT diabetic subgroup data (Cannon et al., 2015) clearly show that a one-every-10 mg/dl reduction in LDL-C will result in proportional cardiovascular benefit, as diabetic patients will have more benefit per unit of LDL-C reduction than non-diabetic patients because of their higher absolute risk. It underscores the importance of ezetimibe, which has recently become available as a generic drug and is well tolerated, as an important but underutilized therapy in the management of dyslipidemia in diabetics. Have you ever thought about not prescribing ezetimibe when statins alone are not enough to meet the target?

11.3 systemetic response

The interventions as a group indicate a need for a systemic (group level) approach to meaningful improvement. The best models include: (1) E-CDS to identify patients who are above target and to encourage interventions; (2) involvement of pharmacist or NP/PA to make sure that interventions are carried out without clinical inertia; (3) patient engagement tools such as shared decision making and medication counseling to enhance adherence; and (4) population-level monitoring of quality and performance feedback to provide accountability. Systems that use more than one component at the same time, like the VA health system, have significantly higher performance, compared to any one component.

11.4 Special Populations

There are a number of sub-groups that will need individual solutions. Decision on secondary prevention should be made on a case-by-case basis for elderly patient because of frailty and life expectancy. Selecting statins that have renal safety profiles is important in patients with CKD. Alternative formulations could be useful for women as they are more prone to SAMS. An integrated care approach is needed for patients with mental health comorbidities. The solutions that are required are at the system level, such as availability of generics, national procurement programmes and task shifting to non-physician providers in patients in low-resource settings. The observation of Mbanya et al. (2020) that less than 25% of those with T2DM in the sub-Saharan Africa receive any statin therapy is a humanitarian failure – as well as a clinical failure.

CONCLUSION

This narrative review has thoroughly outlined the ubiquitous inadequacy of LDL-C management in the T2DM population with dyslipidaemia in all healthcare settings worldwide. The evidence comes together to a set of well described, interacting determinants: systematic underintensifying of statin therapy; clinical inertia at the prescriber level; poor adherence of patients due to a number of factors, including polypharmacy, tolerability concerns and cost issues; dramatic underuse of combination therapy; and wide and very significant geographic, demographic, and socioeconomic differences in prescribing quality. These failures have serious consequences on the cardiovascular system. Because of the high baseline rate of cardiovascular events in people with T2DM, and the linear dose–

response relationship between lowering LDL-C and reducing cardiovascular risk established from statin trials and results from the IMPROVE-IT trial and the FOURIER outcomes study, the current treatment gap at the population level represents a significant number of preventable myocardial infarctions, strokes, and cardiovascular deaths. This is not just a quality measure - it's the imperative to patient safety. Systematic, protocol-driven approaches need to be adopted by clinicians, EHR decision support, pharmacist-led models and telemedicine need to be funded by healthcare systems, and the need to manage LDL-C in the era of newer glucose lowering therapy should be communicated by guideline developers; finally, health policy must address cost and access barriers, especially in low resource settings. Additional studies of implementation science testing multi-component quality improvement interventions and examining inequities based on demographic differences should be prioritized in future studies, as should long-term outcomes studies quantifying the cardiovascular effect at the population level of closing the LDL-C treatment gap in T2DM.

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