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Dyslipidemia: Current Therapies and Strategies to Overcome Barriers for Use

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A B S T R A C T

Dyslipidemia continues to be a major predictor of adverse cardiovascular outcomes in patients with risk factors as well as diagnosed atherosclerotic cardiovascular disease. Recent clinical trials and national guidelines from the US Preventive Services Task Force, American College of Cardiology, and American Heart Association have reinforced a paradigm shift from quantitative reduction of low-density lipoprotein cholesterol targets to prevention and risk factor reduction. Optimized medical therapies have become more inclusive of patients in both the primary and secondary care settings. Although statins continue to be a cornerstone of all recommended therapeutic options, many barriers to patient adherence with medical therapy exist. As medical options change to include the newer lipid-lowering treatments, patient adherence and provider practice challenges can diminish the benefits these medications offer. Although the phenomenon of adherence is complex, multidisciplinary teams, technology, improved communication, prior authorization, step-wise approaches, and the streamlining of the appeal process have shown benefit to mitigate cardiovascular disease-related sequelae. A current overview of practitioner barriers such as organizational restrictions, as well as patient challenges such as poor health literacy and poverty, are examined. Collaborative, multidisciplinary planning and interventions are reviewed with suggestions to increase patient adherence and optimize treatment regimens. This article reinforces existing knowledge while providing new insights to these issues.

This activity is designed to augment the knowledge, skills, and attitudes of nurse practitioners by helping them improve their knowledge of current dyslipidemia therapies and recognize common barriers to treatment compliance.

At the conclusion of this activity, the participant will be able to:

a. Explain in detail at least 2 therapies for dyslipidemia and their basic mechanisms
b. Describe at least 2 common barriers to medication adherence in dyslipidemia patients
c. Evaluate at least 1 strategy for improving patient compliance with treatment plan

The authors, reviewers, editors, and nurse planners all report no financial relationships that would pose a conflict of interest. The authors do not present any off-label or non-FDA-approved recommendations for treatment.

This activity has been awarded 1 Contact Hour of which 1.0 credit is in the area of Pharmacology. The activity is valid for CE credit until Jan 01, 2024.

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Introduction

It has been well documented that patient adherence to lipid-lowering therapies for the treatment of dyslipidemia is associated with a lower risk of adverse cardiovascular outcomes.[1-5] Recent findings of the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial examined strategies for stable coronary artery disease (CAD) and have validated the importance of the role of all treatment options to include aggressive lipid lowering. Although this study showed similar risks for both medical and invasive approaches in cardiovascular deaths, myocardial infarctions (MI), hospitalizations for unstable angina, heart failure, conservative strategies revealed lower risk of procedural MI and hospitalization for heart failure. Invasive strategies revealed lower risks of spontaneous MI, and hospitalizations for unstable angina. These results stress that pharmacological measures are essential to reduce cardiovascular events in both invasive and noninvasive strategies.[5-7] Nurse practitioners (NPs) and all clinicians have a pivotal role in providing structured, systematic care to reduce these events. Many barriers influencing patient adherence to medical strategies—specifically lipid-lower therapies—exist. These barriers and corresponding strategies to improve adherence have also been well documented

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in the literature and endorsed by both national and professional published guidelines. The latest guidelines for the management of cholesterol published in 2018, are from the US Preventive Services Task Force (USPSTF), the American College of Cardiology (ACC), and the American Heart Association (AHA). Despite this, patient adherence to drug therapies remains an obstacle to improving atherosclerotic cardiovascular disease (ASCVD) complications and outcomes.[5] Increased demands on NPs and all clinicians are adding new stressors and limitations to help patients overcome barriers to adherence.[8] This article provides a current overview of practitioner barriers such as organizational restrictions as well as patient challenges such as poor health literacy and poverty. Collaborative, multidisciplinary planning and interventions are examined with suggestions to increase patient adherence and optimize treatment regimens.

Epidemiology

Statistical updates by the Centers for Disease Control and Prevention (CDC) have long maintained ASCVD as the leading cause of death and mortality across the spectrum of sex and race.[9,10] Projections estimate the health care–related financial burden for ASCVD to be $509 billion (about $1,600 per person in the United States) by 2035.[11] These economic burdens include health care services, medication, and lost productivity.[1,12] Although improved initiatives are credited for a 30% decrease in ASCVD deaths, it is still predicted that by 2030, 43.9% of the US adult population will have some form of ASCVD.[13] The CDC also reports that CAD, a subset of ASCVD, is the most common type of all heart diseases.[10,14] Adherence to lipid-lowering options correlates with low-density lipoprotein cholesterol (LDL-C) reduction and risk and has accounted for a yearly reduction of 12,000 avoidable cardiovascular events per 500,000 patients.[15] Poor implementation of prevention strategies and uncontrolled ASCVD risk factors in many adults are the most cited causes of ongoing morbidities relating to cardiovascular disease.[1]

Impact of Trials Drive Current Management of CAD

Multiple studies since 1980, most notably the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial in 2007 through the Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina (ORBITA) trial in 2017, have resulted in published practice guidelines for the management of CAD, which suggest intensive optimal medical therapy (OMT) and lifestyle modifications as first-line therapy.[1,2,16,17] Foundational studies echoed the necessity of OMT and lifestyle modifications with the publication of the ISCHEMIA trial examining asymptomatic stable ischemic heart disease. All studies endorsed the treatment of CAD whether with invasive interventions or conservative options as a complex issue. All therapies include medication adherence, specifically lipid-lowering medications, as a crucial component in the mitigation of ASCVD.[3,8,15,18,19] A systematic review conducted from 2008 and 2015 demonstrated patient adherence initially as only 50% at 1 year, then over time, it can decline even more drastically.[3] The complex challenges regarding the prevention of ASCVD are to minimize risk in both the nonmodifiable aspects of ASCVD (ie, sex, race, familial predisposition) as well as modifiable comorbidities.[20] The most cited modifiable risk factors for heart disease are uncontrolled hypertension, dyslipidemia, and tobacco use.[2] Wide-ranging socioeconomic barriers confound patient adherence. Most often, underlying physical and emotional stressors such as obesity, diabetes mellitus, physical inactivity, poor nutrition, alcohol misuse, poor adherence, lack of social support, and poverty further complicate these barriers.[14] Globally, 82% of ASCVD deaths take place in economically challenged countries and occur equally in either sex.[21] Cost-effective medications such as aspirin, statins, and blood-pressure-lowering agents remain unaffordable for much of the world.[8,9] This article addresses dyslipidemia and options for lipid lowering by focusing on related adherence barriers.

Dyslipidemia

It is not an underestimation to claim that cholesterol plays a vital role in the integrity of all cell membranes. The functions of ingestion, biosynthesis of hormones, absorption, and excretion in lipoprotein dynamics continually changes over the course of a lifetime.[22] Optimal fasting serum values are total cholesterol (TC) <200 mg/dL, high-density lipoprotein cholesterol (HDL-C) >60 mg/dL, LDL-C <100 mg/dL, and very low-density lipoprotein cholesterol (VLDL) <150 mg/dL. However, if CAD is known, then the LDL-C should be <70 mg/dL. Increased atherogenicity is associated with an elevated apolipoprotein B (apoB), LDL-C, and VLDL-C. Approximately half the VLDL particle is made of triglyceride (TG), hence the emphasis on the importance of lowering the level of TG.[2]

Dyslipidemia is defined as any abnormal levels in lipoproteins such as elevated TC, LDL-C, or VLDL-C, as well as low HDL-C. An abnormal level of any of these can be the result of one or more genetic abnormalities or secondary to an underlying disease or environmental factors.[23] The most frequent type of dyslipidemia, also known as secondary dyslipidemia, responds with treatment of the HMG-CoA reductase, the rate limiting (i.e., rate of a reaction) enzyme in the synthetic pathway in cholesterol metabolism.[23] There are genetic outliers defined as a type of autosomal dominant dyslipidemia also referred to as “familial type II disease,” which, if a person is screened in adolescence, can manifest in early childhood. International experts have elaborated that the clinical diagnosis of familial hyperlipidemia (FH) is quantified as LDL-C >190 mg/dL and either a first-degree relative with LDL-C >190–248 mg/dL in 2 subsequent visits or with known premature CAD (women <60 years old and men <55 years old).[24,25] The goal in both types of dyslipidemia is to lower LDL-C, but the mechanisms of treatment may need to be adjusted based on where the impairment of catabolism occurs with FH.[25,26]

Primary Prevention

Proactive universal screening for risk factors in early childhood and adolescence are becoming more commonly addressed in primary prevention. Younger patients taking statins as part of a primary prevention plan unfortunately have the highest rate of nonadherence.[27] Lifestyle changes have been globally accepted as the first measure to change cardiovascular and all-cause mortality and morbidities at any age.[1,2,4,28] Even modest lifestyle changes in diet and exercise can significantly reduce cardiovascular risk markers, such as lipid profiles, inflammatory risk markers, and total body weight.[6,13] Unfortunately, published studies have also demonstrated that long-term adherence with lifestyle changes are initially high but then over time can drastically decline.[18,27,29]

As multiple randomized controlled trials have evolved, most notably the COURAGE trial and ORBITA trial in 2017, guidelines have identified specific groups that would benefit from lipid lowering medications.[13,17,28,30,31] Statin therapy intensity is divided into 3 categories: high, moderate, and low. Each level lowers the LDL-C levels proportionally. Guideline specific doses for each pharmacological agent are listed in Tables 1–3.[2]

Table 1
High Intensity of Statin Doses: Lower Low-Density Lipoprotein ≥50% [2]

Statin	High-Intensity Dose
Atorvastatin	40–80 mg
Rosuvastatin	20–40 mg

In 2018 the USPSTF, ACC, and AHA expanded on the 2013 set of guidelines first proposed by the ACC and AHA becoming more inclusive. These guidelines clearly emphasize pharmacological treatment to include even adults without any history of ASCVD.[2,4] On the basis of results from the Framingham Heart Study concerns for ASCVD regarding age, sex, and the presences of high blood pressure and high cholesterol parsed out a risk-stratification tool called the Framingham Heart Score. Adults aged 40–75 that develop ASCVD risk factors (dyslipidemia, type 2 diabetes, hypertension, or current tobacco use) should have their 10-year risk for an atherosclerotic event evaluated. If their risk is >10%, a low- to moderate-dose statin is recommended.[32] In patients with preexisting cardiovascular pathology without ischemia, the 2018 guidelines transitioned away from LDL-C targets to recommend that all patients younger than 75 years receive high-intensity statin therapy. Patients in this age group that have trouble tolerating the higher doses are recommended to receive moderate-intensity statin therapy. Therapeutic challenges exist, but adherence is critical and should therefore be individualized for each patient.[2]

Secondary Prevention

Later guidelines suggest that, to prevent the recurrence of clinical events in addition to previous nonpharmacological and pharmacological measures, modifications must include the discussion of even more aggressive goals. These goals include a target LDL-C of <70 mg/dL and non-HDL-C <100 with even closer monitoring of response to therapy. Ongoing discussions with patients should include nonstatin therapies, referral to a nutritionist, and other options, which may include LDL-C apheresis.[13] Patients having had a prior MI or with documented presence of plaque by catheterization or computed tomography angiography are considered to have stable CAD. They are asymptomatic or their symptoms are controlled by medications or revascularization.[26,33,34] Invasive therapy is still appropriate for symptomatic CAD, specifically left ventricular ejection fraction <35%, and left main coronary artery stenosis.[6,7]

Lipid-Lowering Options

Over the past 30 years the treatment of dyslipidemia has made significant advances since the first statins appearance in 1989.[4,13,35]

Table 2
Moderate Intensity of Statin Doses: Lower Low-Density Lipoprotein Cholesterol >30%–49%[2]

Statin	Moderate-Intensity Dose
Lovastatin	40–80 mg
Pravastatin	40–80 mg
Simvastatin	20–40 mg
Atorvastatin	10–20 mg
Rosuvastatin	5–10 mg
Pitavastatin	2–4 mg

Table 3
Low Intensity of Statin Doses: lower Low-Density Lipoprotein <30% [2]

Statins	Low-Intensity Dose
Simvastatin	10 mg
Pravastatin	10–20 mg
Lovastatin	20 mg
Fluvastatin	20–40 mg
Pitavastatin	1 mg

Statins

According to the 2018 AHA/ACC Guideline on Management of Blood Cholesterol, statins continue to be the cornerstone of lipid-lowering management.[2] The most frequent type of dyslipidemia responds by decreasing cholesterol synthesis in the liver by inhibiting HMG-CoA reductase. HMG-CoA reductase converts HMG-CoA into mevalonic acid, an important intermediate and precursor to cholesterol synthesis. This results in an increase in the number of LDL-C receptors in the liver, increasing hepatic uptake of LDL-C and thus reducing circulating LDL-C in the blood by up to 50%.[3,36] HDL-C is also known to increase but that mechanism is not well understood but clearly beneficial in preventing future cardiovascular events.[37,38]

Additional benefits of statins include the following:

- New vascular growth via nitric oxide–mediated promotion
- Osteogenic properties
- Decrease LDL oxidative stress (decreased free radical exchange)
- Systemic antiinflammatory effects or pleiotropic effects
- Decreased C-reactive protein levels

All benefits result in plaque stabilization, reversal of endothelial dysfunction, and decreased thrombogenicity.[23]

Available statins listed in Tables 1–3 are usually taken in the evening. Extended-release options are available with fluvastatin and lovastatin.[38] Although each statin has the global benefits previously mentioned, atorvastatin is the first to mitigate the risk of hospitalization in patients with heart failure due to the direct antiinflammatory effects on cardiomyocytes.[23]

The 3 main side effects specific to statins are as follows:

- Transaminitis—significant elevations may cause liver toxicities in susceptible patients
- Myalgias and myopathies due to the release of toxins which in severe cases can cause rhabdomyolysis (destruction of skeletal muscle)
- Moderate increase in diabetes risk

Risk versus benefit regarding reduction of ASCVD events should be considered.[8]

Nonstatin Modifying Agents

As mentioned previously, if statin treatment alone fails to lower LDL-C to <70 mg/dL no–statin-lowering drugs may be employed, especially among patients requiring secondary prevention.[1,39] Often working synergistically, these include ezetimibe, bile acid sequestrants (BAS), and proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors. The 2018 ACC/AHA guidelines suggest TG-lowering drugs such as fibrates and nicotinic acid to target TG levels >175 mg/dL, but not specifically for LDL-C reduction alone.[2]

Table 4
Provider/System Issues and Patient Related Issues

Provider/System Issues	Patient-Related Issues
• Overestimation patients' awareness of disease process[54] • Overestimation of implementation of guidelines in clinical practice[54] • Time constraints in clinical settings hindering guideline implementation and appropriate patient education[55] • Lack the motivation due to ongoing obstructive resistance and lack of adherence on the patients part due to poor health literacy[8] • Prohibitive insurance reimbursement systems[56,57] • Restrictive institutional formularies and hospital policies to optimize clinical practice[56,57] • General practitioners believe that statins are aggressively prescribed in primary prevention; most agree that secondary prevention indications are more valid[54,59] • Statins were less frequently prescribed to females, but women had a higher rate of adherence than men[61] • Socioeconomic areas considered impoverished are associated with higher prescribing rates due to lower health literacy with poorer adherence in both primary and secondary prevention[60] • Burdensome approval process[57]	• Atherosclerotic cardiovascular disease risk perception[19] Health literacy[19] • Concerns regarding both long- and short-term side effects[19] • Cost of treatment[19] • Primary vs secondary prevention[19,58] • Existence of multiple comorbidities[19] • Socioeconomic factors/barriers[60]

LDL Apheresis

Resistant elevation in LDL-C despite maximized medical therapies such as those with severe homozygous or heterozygous FH may qualify for LDL-C apheresis.[40] Apheresis is a treatment option that can be done as either a weekly or biweekly heparinized extracorporeal procedure that directly removes LDL-C from the bloodstream, thereby initially lowering LDL-C by 70%–80%; subsequent treatments sustain a 40% average decrease over a 2-week period.[41]

Future and Newly Approved Therapies

A potential future therapy include inclisiran, a longer acting PCSK9 inhibitor that inhibits hepatic synthesis by interfering with small RNA.[29,33,42] Inclisiran is currently in a phase 3 double-blind trial, and thus is not FDA approved. Newly approved bempedoic acid is an adenosine triphosphate citrate lyase inhibitor that reduces the biosynthesis and upregulates LDL receptor dysregulation in FH.[43–45] The data for these novel lipid-lowering options are promising, but further studies, including long-term studies, are needed to identify patients for whom these drugs are a reasonable therapeutic option.[33]

Adherence

Adherence is described as the extent to which patients take their prescribed medications as directed.[19,46] Nonadherence can be intentional or unintentional. Historically, this metric is complex and has been difficult to measure. Recent studies reveal some of the contextual factors that influence adherence, such as perception of need, concerns regarding side effects or costs, past experiences, and practical difficulties concerning the various options for medications.[46] A Cochrane systematic review in 2016 that included 35 studies and randomized 925,171 participants in a meta-analysis reinforced Vermeire's 2001 conclusions on patient adherence and determined that long-term statin adherence is as low as 25%. Additionally, less than 50% of adherent patients achieve their suggested target cholesterol goals.[12,19,47,48] Predictors of low adherence included poverty, female gender, level of education, race/ethnicity, and age extremes (<50 or >70 years).[19,46]

Barriers

Numerous reasons of medication aversion have been cited from reluctance to swallowing pills to life-limiting myalgia.[8] Somatic intolerances and myalgias to statins are well studied and reported often but a meta-analysis of 27 randomized controlled trials in 2012 by the Cholesterol Treatment Trialists reported serious myopathies, hemorrhagic stroke, and rhabdomyolysis actually occur rarely.[49,50] The exact mechanism for myalgias is poorly understood but thought to be related to the inhibition of mevalonate production in the liver, an important precursor to compounds that maintain the integrity of muscle fibers. Statins have been shown to be safe as well as having addition ASCVD risk-reduction benefits such as plaque stabilization and antiinflammatory effects in both moderate- and high-intensity treatment options, which exceeds any potential harm from statin therapy.[1,2,4,49] The safety profiles of nonstatin modifiers such as ezetimibe, BAS, and PCSK9 inhibitors (as discussed) follow this same risk-reduction benefit.[51,52]

According to the Cumulative Exposure Model barriers to adherence can be broken down to patient related and practitioner/systems related issues.[53] The treatment of an asymptomatic condition such as dyslipidemia poses significant barriers to adherence as listed in Table 4.

Solutions to Adherence Barriers

Population Strategies

Population-level prevention strategies have been shown to benefit risk reduction.[12,13] The World Health Organization goal of globally reducing ASCVD by 25% by 2025 includes several strategies.[62] It has been hypothesized by the European Society of Cardiology (ESC) that population-based strategies to allow statins and other drugs to prevent ASCVD have increased availability and affordability to at-risk communities. Options such as changing the dispensing status of statins from prescription to over-the-counter availability were considered in some countries to combat the problem of under usage. Unfortunately, the ESC described descent from other medical communities, thus allowing prescriptive protocols to remain intact.[8]

Multidisciplinary Teams

As with any treatment, shared decision-making in discovering the most responsible options in both primary and secondary prevention is essential in this population. Multidisciplinary teams consisting of NPs, physicians, nurses, clinical pharmacists, physician assistants, and/or medical assistants have collectively improved practitioner-based outcomes.[57] Team-based care approach is a

Class of Recommendation Level 1 and a Level of Evidence A for the prevention of ASCVD in the 2019 ACC/AHA guidelines.[1]

While teaching is ongoing at each phase of the continuum in both primary and secondary prevention, hospital studies have shown that the timing of teaching patients was perceived as significant with shared decision-making.[55] Future clinical studies may be warranted to possibly identify options for piqued patient engagement because adherence has been shown to improve with the occurrence of a MI or stroke.[19]

Coronary Artery Calcium

To improve the understanding of an individual's current CV risk coronary artery calcium (CAC) testing along with risk stratification tools such as the Agatston score within the context of shared decision is used as a predictor of cardiovascular morbidities.[63] Endorsed by the 2018 ACC and AHA cholesterol treatment guidelines, CAC is suggested for those cohorts who are borderline to intermediate risk, such as asymptomatic individuals aged 40–75 years, no clinical ASCVD, and 10-year ASCVD risk between 5% and 20%, or patients with a strong family history of premature CAD and <5% ASCVD risk. The Society of Cardiovascular Computed Tomography and the Society of Thoracic Radiology Guidelines gave a Class I recommendation for at least qualitative visual CAC scoring on all chest CTs, endorsing it as an excellent method for conveying risk information to patients hesitant to adhere with their medical regimes.[64]

Individualization of Treatment Options

Patients who are fearful of taking statins need to have their individual concerns regarding the true state of their individual ASCVD risk, as well as the efficacy and safety of the suggested treatment options, addressed and tailored to build trust with the NPs and other clinicians involved. Although Schedlbauer et al. cited a 13% improvement in adherence with pharmacist-mediated information using postal and phone reminders, dissatisfaction with the amount of information received about treatment modalities is a prevalent reason cited in qualitative studies.[19,65]

Interestingly, a meta-analysis showed that the number of office provider visits was not a conclusive factor in adherence.[27] Conversely, subsequent studies found increased practitioner "partnership" with seniors to increase the likelihood of medication adherence.[66]

Statin rechallenging has been shown to be a successful method to address the issue of suspected statin intolerance. Statin variations regarding specific agents and or dosing are trialed until a well-tolerated regime is successful.[67] Vonbank et al. offered the opinion that a trial of rechallenge is mandatory in most cases of suspected statin intolerance.[8] Zhang et al. reported that despite the labor-intensive nature in finding the well-tolerated course of treatment, when rechallenging occurs 92% of patients remained adherent more than 1 year later.[68] The measurement of serum cholesterol biannually as well as with treatment changes has provided subjective evidence to both patient and practitioner as to the efficacy of treatment.[19]

The simplification of the drug regimens such as a once- or twice-a-day dosing or the combining of agents into a single pill (polypill) has been shown to improve adherence and risk-factor levels across a wide range of patient groups.[19,62] The newer combined agents such as bempedoic acid and ezetimibe have been approved as adjunct therapy for those patients requiring more aggressive LDL-C control.[45,69] To increase adherence, longer acting PCSK9 inhibitors such as evolocumab and alirocumab can be administered during the office visit.[29] Additional novel approaches including one-time administrations or PCSK9 vaccinations are also hopeful for this drug class.[15]

Although the Internet can, at times, be counterproductive for NPs and other clinicians that are challenged by patients preconceived and ongoing misinformation, online educational resources such as the AHA and lipid association's websites offer patient-friendly tools to increase patients' understanding of heart disease at any phase of the educational continuum.[66] On the practitioner side of the educational option, it can also be helpful to access electronic management tools that can efficiently disseminate guidelines and facilitate decision support. AHA promotes "Get With The Guidelines," an institutional based programs or patient management tools to promote collaborative learning with secondary prevention guidelines.[12] A multidisciplinary team might use technology that enables collaboration with community pharmacies to improve best practice and electronic medical record alerts to clarify issues of concern. These patient-friendly options can also offer scalable low-cost options for pill and refill reminders. These options can be enabled during the support staff portion of a routine visit using mobile apps. PharmD access to prescriptions and refills through electronic health care solutions that connect pharmacies to electronic patient records and enable automated prescriptions have afforded better practitioner options.[15]

Freely available websites such as MedlinePlus are comprehensive and provide easily understandable information for patients.[70] MedlinePlus is also available in Spanish.[71] Tablet-based standardized questionnaires can include questions such as "Are you having any side effects to your medications?" or "Are you having trouble filling your prescriptions and why?" can identify issues proactively thereby increasing office efficiency by having the patient fill it out before the visit or in the waiting room. Patients have the opportunity to answer a couple of key questions on an electronic tablet or paper, which can then be summarized during the initial visit as part of the patient's examination.

Solution-based options to empower patients as well as NPs and other providers to address the barrier of cost include prescription pricing websites such as www.goodrx.com, https://familywize.org/drug-price-look-up-tool, and https://www.wellrx.com/prescriptions/ as affordable options. Private, state, and local institutions often have medication assistance programs. Independent, national organizations such as Patient Access Network, and nonprofits such as Amgen Safety Net Foundation are also venues for financial support. Many pharmaceutical companies often sponsor discount and copay cards.[57]

PCSK9 inhibitors approved with adjunctive therapies in those patients with resistant dyslipidemia have historically been cost prohibitive.[72] In 2018, Amgen aligned with the AHA Value in Healthcare Initiative to reduce the annual cost of their drug evolocumab from greater than $14,100 a year to $5,850.[73] Seventy-nine percent of Medicare Part D and Medicare Advantage plans cover evolocumab at the cost of $25 to $518 since January 1, 2020.[74] Additionally 74% of Medicare Part D and Medicare Advantage plans cover alirocumab at a price of $29 to $618.[75] Documentation for approval can be streamlined with Leverage Tool Form letters that clarify the failure to document issues that plague NPs and other clinicians that have limited time and resources.[57]

Conclusions

Dyslipidemia is a major predictor of adverse CV outcomes in patients with risk factors as well as diagnosed ASCVD. Recent trials and guidelines have reinforced a paradigm shift that has become more inclusive of patients in both the primary and secondary care settings. The focus is now aimed at risk factor reduction rather than quantitative reduction of LDL-C targets. Statins continue to be a

cornerstone of all recommended therapeutic options. As options change to include the newer lipid-lowering treatments, patient nonadherence and practice issues can diminish the benefits these medications offer. While the phenomenon of adherence is complex, multidisciplinary teams, technology, improved communication, prior authorization, stepwise approaches, and the streamlining of the appeal process have shown benefit to mitigate ASCVD-related sequelae. Using the strategies and suggestions described in this article, NPs have an opportunity to improve outcomes by using the strategies presented here.

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