

CLINICAL REVIEWS

Modern Approaches to Dyslipidemia: Integrating Advanced Risk Markers and Imaging in Primary Care

Humza Siddiqi, MD¹, Mahvash Husain, MD¹

¹ Family and Community Medicine, The University of Texas Southwestern Medical Center

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Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of preventable illness and death in the United States, underscoring the importance of effective dyslipidemia management in primary care. While lowering LDL cholesterol continues to be the cornerstone of prevention, modern practice increasingly integrates advanced lipid markers and coronary imaging to refine risk assessment and personalize treatment. This review highlights practical strategies for family physicians, including evaluation of statin intolerance, use of non-statin therapies such as ezetimibe, PCSK9 inhibitors, bempedoic acid, and icosapent ethyl, and the role of lipoprotein(a) [Lp(a)] and apolipoprotein B (ApoB) in risk stratification. Coronary artery calcium (CAC) scoring and coronary CT angiography (CTA) are discussed as complementary tools that guide preventive and diagnostic decision-making. By combining lifestyle modification, pharmacologic therapy, and advanced screening approaches, clinicians can deliver individualized cardiovascular prevention and improve long-term outcomes.

INTRODUCTION

Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of preventable morbidity and mortality in the United States.¹ This review paper provides a comprehensive summary of contemporary dyslipidemia management, emphasizing advanced risk markers and imaging in primary care. While LDL cholesterol reduction is the cornerstone of prevention,² contemporary practice increasingly incorporates advanced lipid markers, novel pharmacotherapies, and coronary imaging tools to better identify high-risk patients and personalize treatment strategies. Family physicians play a central role in early detection and management. This review summarizes modern approaches to dyslipidemia treatment, evaluation of statin intolerance,³ use of non-statin therapies,² and the expanding role of lipoprotein(a) [Lp(a)], apolipoprotein B (ApoB), coronary artery calcium (CAC) scoring,^{4,5} and coronary CT angiography (CTA) in clinical decision-making.^{6,7}

FOUNDATIONS OF DYSLIPIDEMIA MANAGEMENT IN PRIMARY CARE

Lifestyle modification remains the foundation of ASCVD prevention and is essential regardless of pharmacotherapy.¹ Core strategies include weight reduction, increased aerobic and resistance activity, smoking cessation, limiting alcohol, and reducing animal-derived saturated fats. Even modest changes can meaningfully reduce ApoB-containing particles and cardiovascular risk.⁸ Medication management should supplement not replace behavioral interventions.

Non-adherence remains a major barrier to disease treatment, these are influenced by age, sex, ethnicity, health literacy and provider communication.⁹ Solutions are multidisciplinary teams, digital reminders, improved provider education, and patient centered communication strategies. Additionally, barriers to novel lipid lowering therapies include cost, regulatory hurdles, and disparities in healthcare infrastructure.^{10,11}

STATINS: FIRST-LINE THERAPY AND PRACTICAL APPROACHES

Statins remain the most effective, evidence-based therapy for LDL reduction and event prevention. Moderate- to high-intensity statins should be initiated in high-risk patients and titrated to the maximally tolerated dose to achieve LDL goals, ideally <55 mg/dL in very high-risk individuals.²

True statin intolerance is uncommon. Best practices include discontinuing the statin until symptoms resolve, then rechallenging with a different statin at the lowest FDA-approved dose.³ Hydrophilic statins (rosuvastatin, pravastatin) are preferred due to lower CYP3A4 metabolism. If symptoms persist, intermittent dosing with long half-life statins may be considered. To qualify as true intolerance, symptoms must recur with ≥ 2 statins, including one at the lowest dose. Patients may exhibit partial intolerance (low-dose tolerance only) or complete intolerance (symptoms at lowest doses of ≥ 2 statins).¹²

NON-STATIN THERAPIES: EXPANDING THE TREATMENT ARMAMENTARIUM

Non-statin therapies provide important adjuncts for patients who do not achieve LDL goals with statins alone or who exhibit statin intolerance. Ezetimibe, which inhibits intestinal cholesterol absorption, offers modest LDL reduction and event benefit when combined with statins, as shown in the IMPROVE-IT trial.¹² PCSK9 inhibitors are monoclonal antibodies that prevent LDL receptor degradation and can lower LDL to 20–30 mg/dL with demonstrated morbidity and mortality benefit.² Bempedoic acid inhibits cholesterol biosynthesis upstream of HMG-CoA reductase, reducing

LDL by approximately 15% with a low risk of muscle-related side effects.² Finally, icosapent ethyl (purified EPA) lowers triglycerides and has shown event reduction in patients with elevated triglycerides despite statin therapy.²

BEYOND THE STANDARD LIPID PANEL: ADVANCED MARKERS FOR RISK STRATIFICATION

Lipoprotein(a) [Lp(a)] is genetically determined and a strong independent risk factor for CAD, MI, stroke, and aortic stenosis.^{13,14} Testing is recommended once in adulthood, particularly for those with family history or unexplained premature CAD. PCSK9 inhibitors offer modest reductions; emerging agents such as pelacarsen and olpasiran reduce Lp(a) by 80–90% in trials but are not yet FDA-approved.^{15,16}

Apolipoprotein B [ApoB] reflects the number of atherogenic particles and is a superior predictor of risk in diabetes, metabolic syndrome, and hypertriglyceridemia.¹⁷ ACC/AHA guidelines consider ApoB >130 mg/dL a risk enhancer, with a goal of <80–90 mg/dL in high-risk patients.²

CORONARY IMAGING IN PREVENTION AND DIAGNOSIS

Coronary Artery Calcium (CAC) scoring is a non-contrast CT used for primary prevention in asymptomatic adults aged 40–75 years when statin decisions are uncertain.^{4,5} CAC = 0: Very low short-term risk; reasonable to defer statin therapy. CAC 1–99: Statin favored, especially age >55. CAC ≥100: Statins strongly recommended; CAC ≥400 indicates very high risk.^{4,5} Not appropriate for chest pain evaluation or patients with diabetes or LDL >190 mg/dL (already statin-indicated).¹

Coronary CT Angiography (CTA) is a contrast-enhanced CT for evaluating symptomatic patients with suspected CAD. Best for stable chest pain and intermediate pre-test probability. Benefits include identification of stenosis and plaque morphology, a long ‘warranty period’ after a negative CTA, and detection of non-obstructive plaque prompting preventive therapy. Key distinction: CAC is a screening tool for asymptomatic individuals; CTA is diagnostic for symptomatic patients.^{6,7}

CLINICAL INTEGRATION FOR THE PRIMARY CARE PHYSICIAN

A practical workflow is described below in [table 1](#): Start with traditional risk assessment (LDL, HDL, TG, ASCVD calculator). Use advanced markers selectively (ApoB in diabetics/metabolic syndrome; Lp(a) once in lifetime). Apply CAC when statin decisions remain uncertain. Use CTA for symptomatic patients, not screening. Escalate therapy logically: statin → ezetimibe → PCSK9 inhibitor/bempedoic acid. Treat to appropriate intensity, not just numbers.

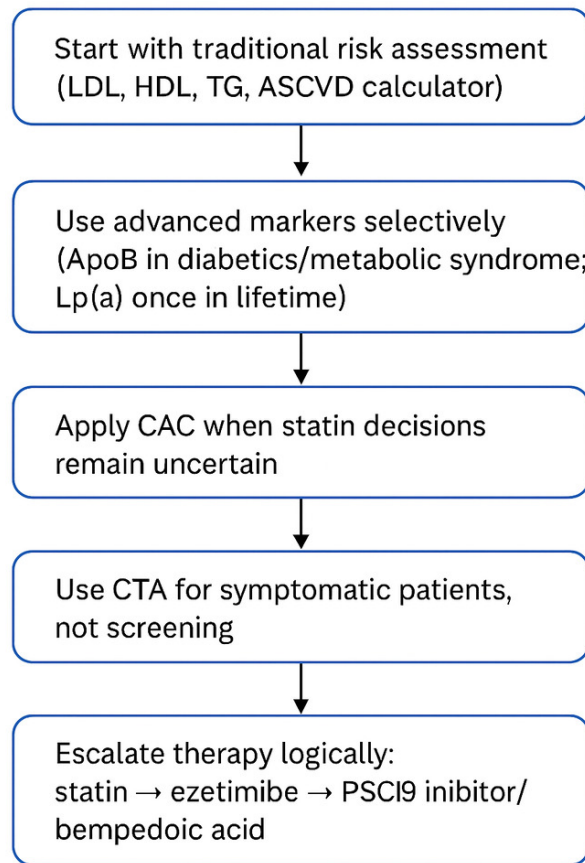


Table 1: Clinical workflow for dyslipidemia management in primary care

CONCLUSION

Modern dyslipidemia management extends beyond the traditional lipid panel. Incorporating advanced markers such as Lp(a) and ApoB, alongside imaging modalities like CAC scoring and CTA, enables clinicians to more accurately identify patients at risk for premature cardiovascular disease. Statins remain first-line therapy, but non-statin options—including ezetimibe, PCSK9 inhibitors, bempedoic acid, and icosapent ethyl—provide effective adjuncts. For family physicians, combining pharmacologic therapy with advanced screening tools allows for precise, individualized cardiovascular prevention and improved long-term outcomes.¹

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SUPPLEMENTARY MATERIALS

clinical workflow

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