Advancing LDL-C Control: Bridging Guideline Targets to Practice

Written by The Life Science Feed Editorial Team · Published 30 August 2026 · Edited by William Lopes

The management of low-density lipoprotein cholesterol (LDL-C) remains a cornerstone of cardiovascular disease prevention. Despite the widespread availability of evidence-based guidelines and effective lipid-lowering therapies, a substantial proportion of patients, particularly those at high and very high cardiovascular risk, do not achieve recommended LDL-C targets. This persistent gap between guideline recommendations and real-world clinical practice presents a significant challenge for healthcare providers, necessitating a re-evaluation of current strategies to optimise patient outcomes.

KEY TAKEAWAYS

- The Pivot: Despite established guidelines and effective therapies, a significant proportion of high-risk patients do not reach LDL-C targets.
- The Data: Real-world data consistently shows suboptimal LDL-C control, with less than 50% of very high-risk patients achieving guideline-recommended targets.
- The Action: Clinicians should proactively intensify lipid-lowering therapy, including combination approaches, to meet individualised LDL-C goals, particularly in high-risk populations.

Current European Society of Cardiology (ESC) guidelines advocate for increasingly stringent LDL-C targets based on individual cardiovascular risk stratification. For patients at very high cardiovascular risk, defined by established atherosclerotic cardiovascular disease (ASCVD), familial hypercholesterolaemia with ASCVD, or severe chronic kidney disease, an LDL-C target of less than 1.4 mmol/L (55 mg/dL) and a reduction of at least 50% from baseline is recommended. For high-risk patients, the target is less than 1.8 mmol/L (70 mg/dL), also with a 50% reduction. These targets are supported by extensive evidence demonstrating a continuous, graded relationship between lower LDL-C levels and reduced cardiovascular event rates. Despite these clear recommendations, real-world observational studies consistently show that a considerable number of patients do not achieve these therapeutic goals. This discrepancy suggests that factors beyond drug efficacy, such as adherence, therapeutic inertia, and patient-specific challenges, contribute to the suboptimal control observed in clinical practice.

Addressing the Treatment Gap

The primary therapeutic strategy for LDL-C reduction involves statins, which are highly effective and well-tolerated. However, many patients require additional lipid-lowering agents to reach their target LDL-C levels, especially those at high and very high risk. Ezetimibe, a cholesterol absorption inhibitor, provides an incremental reduction in LDL-C of approximately 15-20% when added to statin therapy. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors,

such as evolocumab and alirocumab, offer substantial additional LDL-C lowering, typically around 50-60%, when used in combination with statins, or as monotherapy in statin-intolerant patients. These agents have demonstrated significant reductions in major adverse cardiovascular events (MACE) in large-scale clinical trials. Despite the availability of these potent therapies, their uptake and appropriate utilisation in clinical practice remain suboptimal. Data from various registries indicate that less than 50% of very high-risk patients achieve their guideline-recommended LDL-C targets, even with statin therapy. The proportion achieving targets with combination therapy, including PCSK9 inhibitors, is even lower. This suggests a need for improved implementation strategies, enhanced patient education, and more proactive therapeutic intensification by clinicians.

Several factors contribute to the observed treatment gap. Therapeutic inertia, defined as the failure of healthcare providers to initiate or intensify therapy when indicated, is a significant barrier. This can stem from various reasons, including concerns about polypharmacy, potential side effects, patient preference, or a lack of awareness regarding the latest guideline recommendations. Patient adherence to prescribed medications is another critical factor. Poor adherence, often due to complex dosing regimens, perceived side effects, or cost, can significantly compromise treatment effectiveness. Furthermore, the under-recognition of high-risk patient populations and the underestimation of their individual LDL-C goals can lead to insufficient treatment. For instance, patients with diabetes, chronic kidney disease, or a history of premature ASCVD are often not managed to the same aggressive LDL-C targets as those with established ASCVD, despite their elevated risk.

Future strategies to advance LDL-C control must focus on systematic approaches to identify high-risk patients, overcome therapeutic inertia, and improve patient adherence. This includes the implementation of clinical decision support systems, regular audits of LDL-C control rates, and multidisciplinary team approaches. Educational initiatives targeting both clinicians and patients are essential to raise awareness of guideline targets and the benefits of intensive lipid-lowering therapy. The integration of novel therapies, such as inclisiran, a small interfering RNA (siRNA) targeting PCSK9, which offers sustained LDL-C reduction with twice-yearly dosing, may also help address adherence challenges and improve long-term control. However, the successful integration of such therapies into routine practice will depend on clear prescribing pathways, appropriate patient selection, and cost-effectiveness considerations.

> **CLINICAL IMPLICATIONS**
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> The persistent failure to achieve guideline-recommended LDL-C targets in a substantial proportion of high-risk patients is not merely an academic concern; it represents a tangible missed opportunity to prevent cardiovascular events. Clinicians must move beyond the 'set and forget' mentality with statins. The evidence for lower LDL-C translating to better outcomes is unequivocal, and the availability of agents like ezetimibe and PCSK9 inhibitors means there are few justifiable reasons for not intensifying therapy when targets are missed. The argument that patients are 'statin intolerant' often masks a lack of systematic exploration of alternative statins or lower doses, or a reluctance to consider non-statin options.
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> The pharmaceutical industry has delivered highly effective therapies, yet their real-world impact is blunted by underutilisation. Companies developing novel lipid-lowering agents, such as those targeting PCSK9 via siRNA, must continue to provide robust real-world evidence and engage in educational initiatives that address therapeutic inertia directly. The cost-effectiveness of these newer agents, particularly in very high-risk populations, needs to be clearly articulated and supported by health economic data to facilitate broader access

and uptake by healthcare systems.

For patients, this gap means continued exposure to preventable cardiovascular risk. It highlights the need for more active patient engagement in their own care, understanding their individual LDL-C targets, and advocating for appropriate treatment intensification. The responsibility for achieving optimal LDL-C control is shared, but the initial impetus for action often lies with the prescribing clinician. A more proactive, target-driven approach to lipid management, leveraging the full spectrum of available therapies, is not just a guideline recommendation; it is a clinical imperative.

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