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Letter to the Editor

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Reflections on the 2025 ESC/EAS focused update on dyslipidaemia: early LDL-C lowering—between evidence and feasibility

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Dear Editor,

The recently published 2025 ESC/EAS (European Society of Cardiology/ European Atherosclerosis Society) focused update on the management of dyslipidaemias[1] is a significant advancement in cardiovascular prevention. It provides an evidence-based framework that not only redefines the target levels of low-density lipoprotein cholesterol (LDL-C) but also emphasizes the speed at which clinicians should aim to reach these levels. This update is crucial for all healthcare providers involved in cardiovascular risk management, ensuring they are informed and up to date with the latest guidelines.

The 2025 focused update takes a different approach from the 2019 Guideline, which was big and all-encompassing. It does not change the actual LDL-C targets—still <1.4 mmol/L (<55 mg/dl) for very high-risk and <1.8 mmol/L (<70 mg/dl) for high-risk patients. The new document places stronger emphasis on the timing and intensity of lipid-lowering therapy. The central message of the updated document is that both the timing and intensity of lipid-lowering therapy are now considered critical determinants of cardiovascular risk reduction.[2] Achieving LDL-C targets rapidly is emphasized as being as important as the absolute value attained. Table provides a structured comparison of the key conceptual and therapeutic changes introduced in the 2025 focused update relative to the 2019 Guideline.

Risk estimation gets a major update this time. The guideline now formally uses the Systematic COronary Risk Evaluation 2 (SCORE2) and Systematic COronary Risk Evaluation - Older Persons (SCORE-OP) models.[3,4] Relative to the prior guideline approach, which focused only on the fatal 10-year risk, these new models predict both fatal and non-fatal cardiovascular events and adjust for age and region across Europe. The very-high-risk group includes people with established atherosclerotic cardiovascular disease (ASCVD), those with repeat events, diabetics with organ damage, patients with advanced chronic kidney disease, and anyone flagged by SCORE2 or SCORE2-OP as having the highest 10-year risk.

This update improves the accuracy of identifying who is at higher risk, especially among older adults and helps clinicians offer more individualized guidance. On top of that, the 2025 update moves away from the old step-by-step treatment method. Instead of starting with high-intensity statins, then considering ezetimibe, and adding a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor only if needed, the new guideline recommends starting combination therapy early—statin plus ezetimibe—if the patient is at high or very high risk. This strategy enables patients to reach LDL-C targets more rapidly, minimizes

Table. Key differences between the 2019 ESC/EAS guidelines and 2025 ESC/EAS focused update of guidelines for the management of dyslipidaemias

Aspect	2019 ESC/EAS Guideline	2025 ESC/EAS Focused Update
Risk estimation	SCORE system (fatal CVD risk)	Integrates SCORE2 / SCORE2-OP, including fatal and non-fatal events, age- and region-specific calibration
Treatment strategy	Stepwise escalation: statin → +ezetimibe → +PCSK9 inhibitor	Promotes early combination therapy (statin + ezetimibe) in high- and very-high-risk patients
Clinical focus	Emphasis on LDL-C goal values	Shifts toward “time-to-target” and rapid goal attainment
Novel therapies	Introduced PCSK9 inhibitors	Adds bempedoic acid and inclisiran as valid options
Follow-up	LDL-C check at 4–6 weeks post-initiation	Reassessment at 2–4 weeks to expedite adjustments

ESC: European Society of Cardiology, EAS: European Atherosclerosis Society, ACS: Acute coronary syndrome, CVD: Cardiovascular disease, LDL-C: Low-density lipoprotein cholesterol, PCSK9: Proprotein convertase subtilisin/kexin type 9, SCORE2: Systematic COronary Risk Evaluation 2, SCORE2-OP: Systematic COronary Risk Evaluation 2–Older Persons delays in treatment escalation, and may ultimately reduce cumulative atherosclerotic risk—an approach supported by long-term outcome data from clinical trials such as further cardiovascular outcomes research with PCSK9 inhibition in subjects with elevated risk–open-label extension (FOURIER-OLE) and cholesterol lowering via bempedoic acid, an ACL-inhibiting regimen (CLEAR) Outcomes.[5,6]

The update spells out which LDL-C–lowering combinations matter most, especially for high- and very-high-risk groups. High-intensity statin plus ezetimibe is the go-to starting point when patients need a quick, substantial drop in LDL-C. If that is still not enough, or if a patient needs really aggressive lowering fast, triple therapy with a statin, ezetimibe, and a PCSK9 inhibitor comes into play. There is also a role for statin-bempedoic acid combinations if the patient cannot tolerate full-dose statins or is not responding adequately, and inclisiran is an option for tough cases where LDL-C remains stubbornly high. All in all, the field's moving from a slow, stepwise approach to a more proactive, combination-heavy strategy.[7]

The guideline also doubles down on the "time-to-target" approach, particularly in light of recent data from the FOURIER-OLE and CLEAR outcomes trials. The update now recommends initiating intensive lipid-lowering therapy during hospitalization for acute coronary syndrome (ACS), rather than postponing treatment until after discharge. The overarching principle is that achieving lower LDL-C levels earlier is associated with more favorable clinical outcomes.

The 2025 focused update also expands the range of available lipid-lowering therapies. While the 2019 guideline focused primarily on PCSK9 inhibitors, the 2025 update incorporates bempedoic acid and inclisiran, offering additional options for patients who cannot tolerate statins or who continue to have elevated LDL-C despite standard treatment. With these additions, RNA-based and enzyme-targeted therapies have become more integrated into routine clinical practice. The update also adds a new recommendation for evinacumab in patients with homozygous familial hypercholesterolaemia aged 5 years and older who continue to exceed LDL-C targets despite maximally tolerated therapy. This expands the therapeutic options available for a group with some of the most severe lipid disorders.

One more thing: measuring lipoprotein(a) [Lp(a)] is now a much stronger recommendation, especially for patients with early-onset atherosclerosis or a family history of ASCVD. It used to be optional, but now Lp(a) is recognized as an independent, causal risk factor for ASCVD—and possibly a target for future treatments.[8]

The 2025 ESC/EAS focused update sticks with the follow-up schedule set in 2019, so clinicians still check LDL-C about 4 to 6 weeks after starting or adjusting lipid-lowering therapy. This interval allows clinicians to assess the patient's initial response and to adjust therapy when LDL-C targets have not been achieved. The update emphasizes achieving LDL-C targets more quickly, yet the practical monitoring interval remains unchanged at 4–6 weeks. The aim is to maintain consistency in follow-up timing while encouraging more timely adjustments when treatment response is inadequate.

The update puts a spotlight on certain high-risk groups, especially people with HIV (PWH). They face a substantially higher risk of ASCVD due to chronic inflammation, the lipid effects of antiretroviral therapy, and the tendency of standard risk calculators to underestimate cardiovascular risk in this population. For PWH aged 40 and older, the new guidance backs statin therapy for primary prevention, drawing on the randomized trial to Prevent Vascular Events in HIV (REPRIEVE)[9] trial results. If more LDL-C lowering is needed, the update also supports adding ezetimibe or PCSK9 inhibitors. Cancer patients treated with anthracycline-based chemotherapy make up another group with greater cardiovascular risk—cardiotoxicity is a well-recognized concern in this setting. Findings from randomized trials—particularly the Statins to Prevent the Cardiotoxicity of Anthracyclines (STOP-CA)[10] study—indicate that statins may offer cardioprotection in this context. However, results from smaller studies have been less consistent. Following the 2022 ESC cardio-oncology recommendations, the update recommends statins for patients at high or very high risk of cancer treatment–related cardiac problems.[11]

Lifestyle changes still matter, but the update goes further, calling out the influence of social determinants of health and the importance of team-based care. It recognizes that medication alone does not guarantee good outcomes—real-world factors such as support systems, socioeconomic status, and access to care shape adherence and outcomes.

In short, the 2025 focused update keeps the same LDL-C targets as before but shifts the mindset. The question is not just "How low can we go?" but "How fast can we get there?" This new focus shows up in recommendations for early use of combination therapy, novel lipid-lowering drugs, and faster follow-up. Altogether, these changes push lipid management toward modern preventive cardiology, urging clinicians to bridge the stubborn gap between research and everyday practice.

ETHICAL DECLARATIONS

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This letter was externally peer-reviewed.

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