



EAS Updates

News from ESC congress 2019: New ESC/EAS guidelines for dyslipidaemia management published[☆]



Jane Stock

European Atherosclerosis Society, World Trade Center Göteborg, Mössans Gata 10, SE-412 51, Göteborg, Sweden

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It has been three long years since the last Joint European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) dyslipidaemia guidelines were published [1]. In the interim, major clinical trials have demonstrated the efficacy of PCSK9 monoclonal antibody therapies in reducing low-density lipoprotein cholesterol (LDL-C) levels beyond those attained on intensive statin treatment, resulting in significant reduction in cardiovascular events in patients with established atherosclerotic cardiovascular disease (ASCVD) and acute coronary syndrome (ACS) [2,3]. Importantly, there appeared to be no LDL-C threshold for clinical benefit [4]. A subsequent slew of subgroup analyses of the FOURIER and ODYSSEY OUTCOMES trials provided key insights to aid clinicians in targeting treatment to those patients at highest absolute cardiovascular risk, who are likely to benefit most from the addition of a PCSK9 inhibitor. Specifically, very high-risk individuals with recurrent events, more extensive atherosclerotic cardiovascular disease or higher global cardiovascular risk scores are likely to be key targets for the use of PCSK9 inhibitors in clinical practice [5–9].

Additionally, there has been further information from the IMPROVE-IT trial with ezetimibe, which demonstrated enhanced absolute cardiovascular benefit in very high-risk individuals with diabetes compared with those without, reflecting the higher absolute risk of this group [10].

Moreover, knowledge of the impact of genetic variants influencing LDL-C levels and lifelong risk for ischaemic heart disease has increased, driven largely by insights from Mendelian randomisation studies [11,12]. Would treating patients earlier ultimately lead to reduction in risk of the clinical complications of ASCVD? [13,14].

The 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk, were published on 31 August, at the start of the ESC Congress, held jointly with the World Congress of Cardiology in Paris, France [15]. The key question for clinicians is what is new— has recent trial evidence been translated to these guidelines?

1. What's new in the guidelines: LDL goals in high and very high-risk patients

Low-density lipoprotein (LDL) cholesterol levels should be lowered as much as possible to prevent cardiovascular disease, especially in high and very high-risk patients (see Table 1 for patients now included in these categories). It is recommended that very high-risk patients (in both primary and secondary prevention) should achieve both a target LDL-C level of < 55 mg/dL or < 1.4 mmol/L **and** at least 50% reduction from baseline LDL-C levels. In high-risk patients, the LDL-C goal is < 70 mg/dL or < 1.8 mmol/L **and** at least 50% reduction from baseline LDL-C levels. These goals reinforce the view that the lower the LDL-C level, the better for prevention of CV outcomes in these very high-risk patients.

New to the guidelines is recognition that ACS patients are at very high risk of recurrent events. If patients experience a second vascular event within 2 years (not necessarily of the same type as the first event) on maximally tolerated statin therapy, an LDL-C goal of < 1.0 mmol/L (< 40 mg/dL) may be considered.

With recommendation of these new lower LDL-C goals in very high risk and high-risk patients, the ESC/EAS guidelines group have

[☆] The 2019 Joint European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) Dyslipidaemia Guidelines were released on 31 August during the ESC Congress, Paris, France. What were the key changes to those last published in 2016?

E-mail address: office@eas-society.org.

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Table 1

High and very high-risk patients included in 2019 ESC/EAS dyslipidaemia guidelines. What's new in the guidelines: Increased focus on combination therapy.

Very high risk	<ul style="list-style-type: none"> • Documented ASCVD, either clinical or unequivocal on imaging (i.e. previous ACS, stable angina, coronary revascularisation, stroke and transient ischaemic attack, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan defined by multivessel coronary disease with two major epicardial arteries having > 50% stenosis or on carotid ultrasound). • Diabetes mellitus (DM) with target organ damage, ≥ 3 major risk factors or early onset of type 1 DM of long duration (> 20 years). • Severe chronic kidney disease (eGFR < 30 mL/min/1.73 m²) • Calculated SCORE $\geq 10\%$ for 10-year risk of fatal CVD. • FH with ASCVD or with another major risk factor.
High risk	<ul style="list-style-type: none"> • Markedly elevated single risk factors, in particular total cholesterol > 8 mmol/L (> 310 mg/dL), LDL-C > 4.9 mmol/L (> 190 mg/dL), or blood pressure $\geq 180/110$ mmHg. • Patients with FH without other major risk factors. • Patients with DM without target organ damage*, with DM duration ≥ 10 years or another additional risk factor. • Moderate CKD (eGFR 30–59 mL/min/1.73 m²). • A calculated SCORE $\geq 5\%$ and < 10% for 10-year risk of fatal CVD.

Table 2

Summary of other new ESC/EAS dyslipidaemia guideline recommendations.

<ul style="list-style-type: none"> • Cardiovascular imaging for assessment of ASCVD risk <p>Assessment of arterial (carotid and/or femoral) plaque burden on arterial ultrasonography, and CAC score assessment with CT should be considered as a risk modifier in individuals at low to moderate risk.</p> <ul style="list-style-type: none"> • Treatment of dyslipidaemia in older patients <p>Treatment with statins is recommended for primary prevention, according to the level of risk, in older people aged ≤ 75. A statin may be considered for primary prevention in older people aged > 75, if at high risk or above.</p> <p>Statin treatment should be started at a low dose if there is significant renal impairment and/or if there is potential for drug interactions, and then titrated upwards to achieve LDL-C treatment goals.</p> <ul style="list-style-type: none"> • Pre-menopausal women with DM <p>Statin therapy is not recommended in pre-menopausal patients with DM who are considering pregnancy or not using adequate contraception.</p>
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emphasised the importance of combination treatment, first with ezetimibe and then a PCSK9 inhibitor to achieve these targets. In patients with ACS, adding a PCSK9 inhibitor early after the event (if possible, during hospitalisation) should be considered. In these patients, if the LDL-C goal is not achieved after 4–6 weeks despite maximally tolerated statin therapy and ezetimibe, a PCSK9 inhibitor is recommended.

2. What's new in the guidelines: n-3 polyunsaturated fatty acids (n-3 PUFAs – fish oils) in triglyceride management

While statin treatment remains the first choice for managing high triglycerides (TG, > 200 mg/dL or 2.3 mmol/L), the new guidelines have taken account of evidence from REDUCE-IT [16] for n-3 PUFAs (particularly icosapent ethyl 2 × 2 g daily) in high-risk patients with persistently elevated TG (between 135 and 499 mg/dL or 1.5 and 5.6 mmol/L) despite statin treatment. In high-risk patients at LDL-C goal with TG > 200 mg/dL or > 2.3 mmol/L, fenofibrate or bezafibrate may be considered in combination with statins.

3. What's new in the guidelines: importance of lipoprotein(a)

With a substantial body of evidence from epidemiologic and Mendelian randomisation studies supporting lipoprotein(a) [Lp(a)] as causal in ischaemic heart disease [17], the ESC/EAS guidelines recommend Lp(a) measurement at least once in all adults. The guidelines have emphasised that individuals with very high Lp(a), indicative of an inherited lipid disorder, are likely to have a lifetime ASCVD risk similar to that of individuals with heterozygous FH. The new emphasis on Lp(a) is important, given the fact that novel treatments that are specific to this lipoprotein abnormality are now entering phase III clinical trials in high and very high-risk patients. Current options for treatment of high Lp(a) are limited to the PCSK9 inhibitors which have been shown to reduce levels by 25–30% on average, with or without background statin therapy (see Table 2).

4. Concluding remarks

These new ESC/EAS dyslipidaemia guidelines emphasise that lower LDL-C is better. Evidence from Mendelian randomisation studies has been critical in driving a 'sea change' to treat earlier, which ultimately may mean less intensive therapy in the longer-term. With the new LDL-C goals comes recognition of the importance of combination therapy in high and very high-risk patients, first with ezetimibe and then a PCSK9 inhibitor, to attain these levels. The fundamental next steps are appropriate implementation by clinicians in their practice, together with ensuring treatment adherence by patients.

Declaration of competing interest

The author declared she does not have anything to disclose regarding conflict of interest with respect to this manuscript.

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