



Contents lists available at ScienceDirect

## The American Journal of Cardiology

journal homepage: [www.elsevier.com/locate/ajc](http://www.elsevier.com/locate/ajc)

# 2025 ESC/EAS Dyslipidemia Guidelines Focused Update: Intensifying Prevention, Risk Stratification, and Therapy

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## ARTICLE INFO

## Article History:

Received 25 January 2026

Revised 15 February 2026

Accepted 22 February 2026

The 2025 Focused Update of the European Society of Cardiology and European Atherosclerosis Society (ESC/EAS) Guidelines for the management of lipid disorders marks a significant evolution in cardiovascular disease (CVD) prevention, reflecting contemporary evidence, advances in risk assessment, and the advent of novel therapeutic modalities. Dyslipidemia remains a primary modifiable risk for atherosclerotic cardiovascular disease, necessitating robust, evidence-driven strategies to optimize prevention. Notably, the update transitions from the traditional SCORE system to the more comprehensive SCORE2 and SCORE2-OP risk models for estimating 10-year atherosclerotic cardiovascular disease risk. These new models broaden applicability, encompassing both fatal and non-fatal cardiovascular events and extending risk calculation up to age 89, while recalibrating country-specific risk clusters and prioritizing non-HDL cholesterol over total cholesterol as a core indicator. The guidelines emphasize the intensification of therapy for individuals identified as being at higher risk, integrating recent clinical trial data and targeted drug selection, with a particular focus on individualized risk stratification. This focused update contrasts its recommendations against the 2019 standard, outlining the rationale for new strategies in both primary and secondary prevention through intensified lipid-lowering therapy. Comprehensive implementation of these recommendations is anticipated to drive further reductions in ASCVD events, aligning with global public health priorities. The 2025 guidelines thus serve as an essential tool for clinicians and researchers, supporting nuanced decision-making and reinforcing the central role of lipid management in contemporary cardiovascular risk reduction.

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1 Dyslipidemia continues to be a primary modifiable risk factor for  
2 atherosclerotic cardiovascular disease (ASCVD). Following pivotal  
3 trial results and emerging therapies since 2019, the ESC/EAS has  
4 revised its recommendations regarding risk stratification, drug selection,  
5 and treatment intensity to maximize preventive benefit.

## 6 Cardiovascular Risk Stratification

### 7 Transition from SCORE to SCORE2: Redefining ASCVD risk assessment

8 The 2019 guidelines recommended estimation based on the  
9 SCORE (Systematic Coronary Risk Estimation) model, using total cho-  
10 lesterol, HDL, age, sex, and blood pressure; focused mainly on fatal  
11 CVD events and up to age 70.<sup>1</sup>

The major revision is the adoption of SCORE2 and SCORE2-OP risk  
models, replacing the previous SCORE system for estimating the 10-  
year risk of ASCVD events. SCORE2 is recommended for adults aged  
70 years or younger, while SCORE2-OP is applicable for those aged 70  
to 89 years (Class I, Level B). While the SCORE algorithm assessed the  
10-year risk of fatal CVD in persons aged up to 70 years, the SCORE2/  
SCORE2-OP algorithms (accessible at) can also estimate the 10-year  
risk for both fatal and non-fatal CV events, including those in appar-  
ently healthy people aged 70 years or older (up to 89 years). The  
models are calibrated for 4 country risk clusters and use non-HDL  
cholesterol as a risk input, rather than total cholesterol.<sup>2</sup>

In this update, a 2× multiplier was applied to convert previous  
SCORE-based thresholds into SCORE2- or SCORE2-OP-based thresh-  
olds, defining different categories of total CVD risk.

### Revised risk categories and modifiers for personalized care

Updated risk categories are provided for primary prevention,  
encompassing definitions of risk categories based on SCORE2/

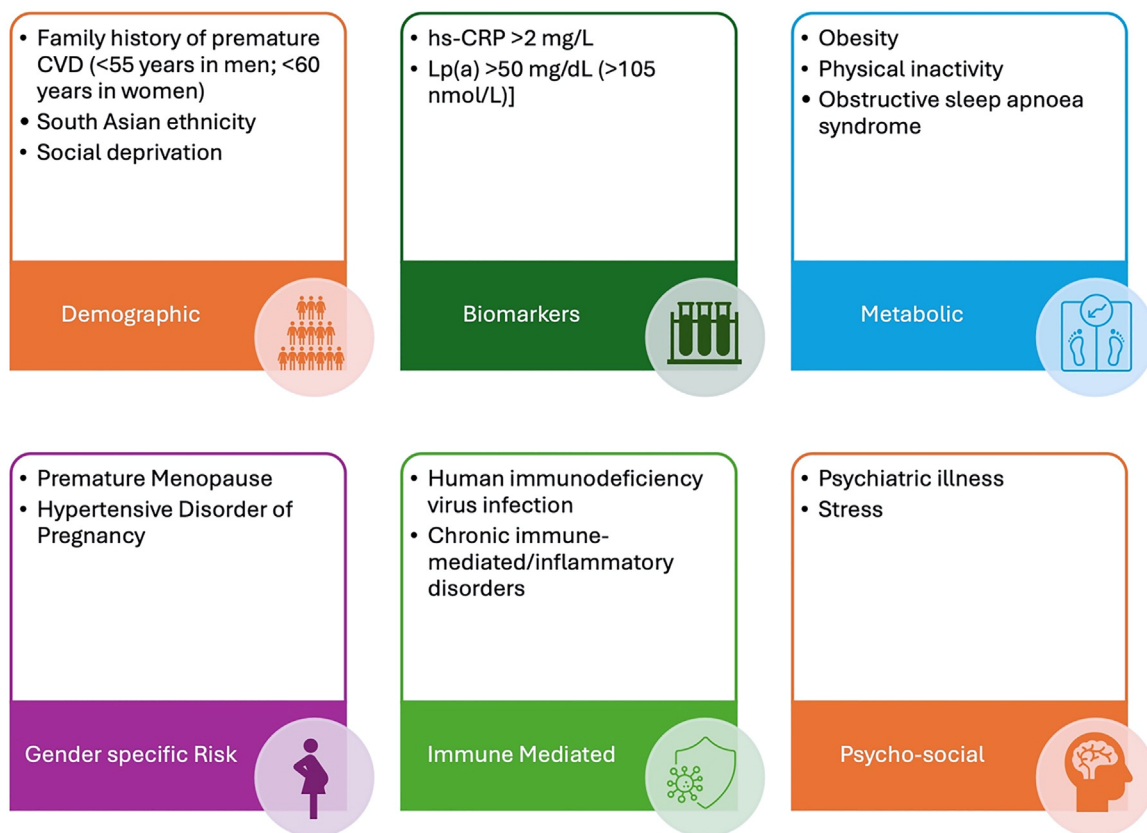
Funding: None.

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<https://doi.org/10.1016/j.amjcard.2026.02.059>

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**Figure 1.** Risk modifiers for consideration beyond the risk estimation based on the SCORE2 and SCORE2-OP algorithms.<sup>1</sup>

Abbreviations: CVD = cardiovascular disease; hs-CRP = high sensitivity C-reactive protein; Lp(a) = lipoprotein(a).

29 SCORE2-OP thresholds. **Figure 1** lists risk modifiers, including demo- 58  
30 graphic, clinical, and biomarker-based variables such as family history, 59  
31 high-risk ethnicity, chronic inflammatory diseases, elevated hs- 60  
32 CRP, and Lp(a) levels of 50 mg/dL or above ( $\geq 105$  nmol/L). The detec- 61  
33 tion of subclinical atherosclerosis by imaging or an elevated coronary 62  
34 artery calcium (CAC) score should be regarded as a risk modifier, par- 63  
35 ticularly for those at moderate risk or those near treatment thresh-  
36 olds (Class IIa, Level B). CAC scoring—very high scores ( $>300$ ) in  
37 apparently healthy people may reclassify risk to an equivalent of sec-  
38 ondary prevention. In contrast, a score of zero indicates lower risk,  
39 even in the presence of traditional risk factors (with caveats for  
40 statin-treated patients as the therapy is known to enhance calcium  
41 deposition in plaques).<sup>3</sup>

42 Premature menopause and hypertensive disorders of pregnancy  
43 (such as pre-eclampsia) as risk factors in the 2025 ESC/EAS lipid  
44 guidelines are supported by growing evidence that these conditions  
45 significantly increase a woman's lifetime risk of ASCVD.

- 46 • Premature menopause is associated with adverse changes in 58  
47 lipid profiles and a higher risk of cardiovascular disease due to 59  
48 the loss of protective estrogen earlier in life. This hormonal 60  
49 change leads to increased levels of LDL cholesterol and triglycer- 61  
50 ides, as well as changes in lipoprotein subfractions, which accel- 62  
51 erate atherosclerosis. 63
- 52 • Hypertensive disorders of pregnancy, including pre-eclampsia, 64  
53 are recognized as significant risk markers for future cardiovascu- 65  
54 lar disease. These disorders reflect endothelial dysfunction and 66  
55 systemic vascular damage during pregnancy, which increases 67  
56 long-term risk for hypertension, ischemic heart disease, and 68  
57 stroke. 69  
70  
71

Because traditional risk prediction models like SCORE2 and SCORE2-OP do not fully recognize the increased cardiovascular risk associated with these female-specific conditions, the guidelines include them as risk modifiers to enhance the accuracy of cardiovascular risk assessment and support more personalized preventive strategies, including lipid-lowering therapy.

*Risk assessment algorithm: Integrating biomarkers and imaging into risk calculations*

Risk stratification now involves a more nuanced approach, integrating imaging and biomarker data alongside traditional risk factors to facilitate personalized management strategies. Calculation of risk with SCORE2/SCORE2-OP should not be performed in those with established ASCVD, diabetes mellitus, chronic kidney disease, or those already on lipid-lowering therapies.

### LDL-Cholesterol Targets and Therapeutic Strategy: Reinforcing Targets and Intensifying Risk-Based LDL-C Lowering

The 2025 update reaffirms the risk-based approach to lowering LDL-C, with the same treatment targets as the 2019 guideline. It re-emphasizes the use of both SCORE2/SCORE2-OP and baseline LDL-C for decision-making, particularly in primary prevention for non-statin candidates.

The LDL-C targets for each risk group are unchanged<sup>1</sup> (Table 1).

The initiation of pharmacological therapy is stratified based on risk assessment and baseline LDL-C levels. However, recent updates emphasize the importance of achieving both absolute and percentage reductions, with a decrease of  $\geq 50\%$  from baseline remaining pivotal

**Table 1**  
LDL-C treatment goals by risk categories

Risk category	LDL-C goal	Class
Low risk	<3.0 mmol/L (<116 mg/dL)	IIb
Moderate risk	<2.6 mmol/L (<100 mg/dL) and $\geq$ 50% reduction from baseline	IIa
High risk	<1.8 mmol/L (<70 mg/dL) and $\geq$ 50% reduction from baseline	I
Very high risk	<1.4 mmol/L (<55 mg/dL) and $\geq$ 50% reduction from baseline	Ia
Extreme risk	<1.0 mmol/L (<40 mg/dL) and $\geq$ 50% reduction from baseline	IIb

84 for patients classified as high- and very-high-risk. A stepwise  
85 approach, aligning LDL-C levels with overall cardiovascular risk, con-  
86 tinues to underpin therapeutic decision-making.

### 87 Innovations In LDL-C Lowering Therapies: Bempedoic Acid, 88 Inclisiran, Evinacumab, and Algorithmic Approaches

89 Both guidelines specify that statins are the primary treatment  
90 choice for the majority of patients.

91 In 2019, non-statin therapies, such as ezetimibe and PCSK9 inhibi-  
92 tors, were recommended for patients categorized as high or very high  
93 risk who are unable to tolerate statins or fail to achieve their target  
94 lipid levels. PCSK9 inhibitors were explicitly emphasized for those at  
95 very high risk, including individuals with a history of acute coronary  
96 syndrome (ACS) and familial hypercholesterolemia.<sup>1</sup>

#### 97 Bempedoic acid

98 ATP-citrate lyase inhibitor bempedoic acid is now recommended  
99 for patients unable to tolerate statin therapy (Class I, Level B) and as  
100 an add-on to maximally tolerated statins (with or without ezetimibe)  
101 for high- or very-high-risk patients who are unable to achieve their  
102 LDL-C goal (Class IIa, Level C). The CLEAR Outcomes study showed a  
103 13% decrease in major adverse cardiovascular events (MACE) com-  
104 pared to placebo in a statin-intolerant group. Safety considerations  
105 include reversible increases in uric acid, a higher risk of gout, and  
106 potential hepatic enzyme elevations.<sup>4</sup>

#### 107 Evinacumab

108 For homozygous familial hypercholesterolemia (HoFH), evinacu-  
109 mab (an ANGPTL3 inhibitor) is recommended for patients aged  
110 5 years or older who have not reached their LDL-C goal despite maxi-  
111 mum conventional therapy (Class IIa, Level B).<sup>5</sup>

#### 112 Inclisiran and other agents

113 Inclisiran, a siRNA targeting PCSK9 synthesis, administered bian-  
114 nually, achieves ~50% LDL-C lowering in Phase III trials; however, its  
115 routine use awaits the results of large cardiovascular outcome trials,  
116 expected in 2026 to 2027. PCSK9 monoclonal antibodies and ezeti-  
117 mibe remain integral to combination therapy for patients who do not  
118 achieve targets with statin monotherapy.<sup>6</sup>

119 Algorithmic, early combination therapy in ACS is explicitly  
120 endorsed.

### 121 Intensive Lipid-Lowering in Acute Coronary Syndromes: “Strike 122 Early and Strong”

123 Patients with acute coronary syndromes (ACS) face the highest  
124 risk for recurrent cardiovascular events in the early postevent period.  
125 Yet, real-world studies repeatedly reveal under-treatment and clinical  
126 inertia after hospital discharge.

The 2025 Update, strengthened by evidence from trials like  
IMPROVE-IT<sup>7</sup>, HUYGENS<sup>8</sup>, PACMAN-AMI<sup>9</sup>, SWEDEHEART<sup>10</sup> and AT-  
TARGET IT<sup>11,12</sup> recommends immediate, in-hospital initiation of  
intensive lipid-lowering therapy for all ACS patients, aiming for “the  
sooner, the lower, the better.”

#### 133 Protocol

- 134 • For all ACS patients, high-intensity statin therapy should be initi-  
135 ated promptly during the hospital stay.
- 136 • For those unlikely to achieve LDL-C targets with a statin alone  
137 (particularly patients already on a statin at admission), add-on  
138 non-statin agents (primarily ezetimibe) should be initiated  
139 before discharge.
- 140 • These recommendations are classified as Class I (statin intensifi-  
141 cation) and Class IIa (statin plus ezetimibe combination for those  
142 not previously treated).

143 The proactive approach ensures maximum early benefit, counter-  
144 acts prescription inertia, and aims to shrink the post-ACS “risk win-  
145 dow.” The guidelines emphasize that aggressive LDL-C lowering is  
146 well tolerated and yields significant outcome benefits if initiated  
147 without delay.

148 The expert analysis emphasizes that systematized protocols, hos-  
149 pital-based lipid clinics, and robust discharge planning are essential  
150 to translating these recommendations into durable clinical benefits,  
151 thereby reducing the persistent care gap after ACS.

### 152 Lipoprotein(a): From Single Measurement to Pivotal Risk Modifier

153 The 2019 ESC/EAS guidelines recommended that Lp(a) levels  
154 should be measured at least once in a lifetime, if possible, to identify  
155 those with a significantly elevated inherited Lp(a) level of 180 mg/dL  
156 or more (430 nmol/L or more). These individuals have a significantly  
157 higher lifetime risk of ASCVD, similar to the risk linked to heterozy-  
158 gous familial hypercholesterolemia (HeFH).<sup>1</sup>

159 The 2025 update recommends that lipoprotein(a) [Lp(a)] be mea-  
160 sured at least once in all adults, especially those with familial hyper-  
161 cholesterolemia, premature atherosclerotic cardiovascular disease  
162 (ASCVD), or at moderate risk or treatment thresholds. An Lp(a) level  
163 of  $\geq$ 50 mg/dL ( $\geq$ 105 nmol/L) is now recognized as a significant risk  
164 modifier that may warrant reclassification and more aggressive LDL-  
165 C lowering strategies (Class IIa, Level B) based on current epidemio-  
166 logical and genetic evidence indicating increased risks of ASCVD and  
167 aortic valve stenosis at these levels. Furthermore, emerging RNA-  
168 based therapies targeting Lp(a) are currently being studied.<sup>13</sup> Mea-  
169 surement of Lp(a) is influenced by substantial structural heterogene-  
170 ity in apolipoprotein(a) isoforms, particularly variability in Kringle-IV  
171 repeats, which may affect assay accuracy.<sup>14</sup> Therefore, the use of apo  
172 (a) isoform-insensitive immunoassays calibrated against interna-  
173 tional reference standards is recommended to ensure reliable quanti-  
174 fication and comparability across studies.<sup>15</sup> The ESC/EAS 2025 update  
175 prefers reporting Lp(a) in nmol/L, as this reflects molar particle con-  
176 centration and is less affected by isoform variability than mg/dL,  
177 which represents mass concentration; accordingly, routine conver-  
178 sion between units is discouraged due to assay-dependent variability.  
179 However, for clinical purposes, mg/dL remains acceptable and clini-  
180 cally interpretable when used with validated, standardized assays.

### 181 Hypertriglyceridemia: Targeted Therapies and Updated 182 Indications-Icosapent Ethyl, Volanesorsen

183 Statins remain the first-choice drugs to reduce CV risk for those  
184 with high triglycerides.

185 *Icosapent ethyl* (2 g twice daily) is now uniquely recommended  
186 —when added to statin—in high or very high risk patients if TG  
187 135 to 499 mg/dL persists, based on REDUCE-IT results (Class IIa,  
188 Level B).<sup>16</sup>

189 *Volanesorsen* (antisense inhibitor of ApoC-III): Recommended for  
190 severe hypertriglyceridemia due to familial chylomicronemia syn-  
191 drome (FCS) when refractory to standard therapy (EMA approval; not  
192 FDA approved) (Class IIa, Level B).<sup>17</sup>

193 *Fibrates and combined (icosapentaenoic acid and docosahexaenoic*  
194 *acid) n-3 PUFA (omega-3 polyunsaturated fatty acids) supplements* are  
195 not broadly recommended for CV event reduction, given negative or  
196 neutral outcome data since 2019 (Class IIb).

### 197 Primary Prevention in HIV: Expanding Statin Indications

198 In 2019, statin therapy was considered for patients living with HIV  
199 (PLHIV) with dyslipidemia who are at high risk of cardiovascular dis-  
200 ease; however, data in this regard remain limited.<sup>1</sup>

201 Following the REPRIEVE trial,<sup>18</sup> which demonstrated a 35% reduction  
202 in MACE, the 2025 Focused Update guidelines introduce a novel  
203 primary prevention strategy. This update recommends statin therapy  
204 for people with HIV (PWH) aged 40 years or older, irrespective of  
205 their baseline LDL-C level. Pitavastatin is recommended explicitly  
206 due to its minimal interaction with antiretroviral therapy.

207 Statins now stand as the only lipid-lowering class with proven  
208 outcome benefits in primary prevention for PWH, distinct from other  
209 agents such as ezetimibe or PCSK9 inhibitors.

### 210 Cancer Patients Receiving Anthracyclines: Statins in Oncologic 211 Care

212 Statins ought to be considered for patients identified as having a  
213 high or very high risk of developing cardiovascular toxicity associated  
214 with chemotherapy, particularly with anthracycline-based regimens,  
215 to mitigate the risk of cardiac dysfunction (Class IIa, Level B) based on  
216 the STOP-CA trial and meta-analyses.<sup>19</sup>

217 There is no similar recommendation for nonstatin therapies due  
218 to a lack of evidence on outcomes. The 2019 update lacked any spe-  
219 cific recommendations in this regard.

### Dietary Supplements: Negative Recommendation

221 The guidelines explicitly discourage the use of dietary supple-  
222 ments or vitamins (including red yeast rice, phytosterols, and generic  
223 n-3 PUFAs) for reducing ASCVD risk, given the lack of robust efficacy  
224 and, in some cases, evolving safety concerns and regulatory restric-  
225 tions. Yet, dietary supplements with proven LDL-C reduction efficacy  
226 and safety may be considered. High-dose, purified icosapent ethyl  
227 remains the exception with proven benefit in specific subgroups  
228 (Class III, Level B).<sup>20</sup>

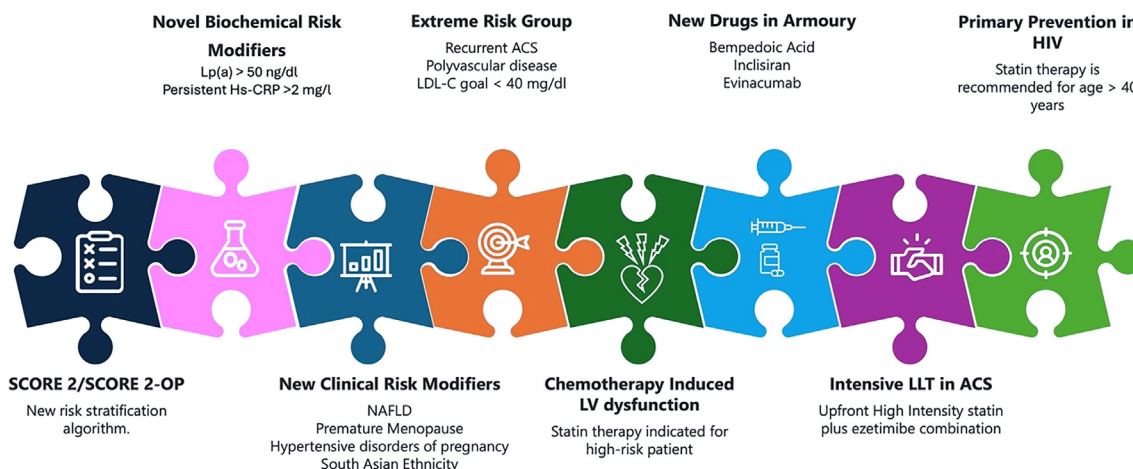
### Practical Implications

- *Shift to improved risk stratification:* Use of modernized, validated risk algorithms for primary prevention; encourage more personalized risk assessment.
- *Combination lipid-lowering:* Accelerated, more intensive post-ACS approach for high event-risk period.
- *Nonstatin therapy:* More robust recommendations and new agents for statin intolerance, familial hypercholesterolemia, and severe hypertriglyceridemia.
- *Special conditions:* HIV, oncology patients, and those with high Lp(a) are addressed more specifically and forcefully.
- *Supplements:* Clear advice against most supplements for ASCVD prevention.
- *Regarding ongoing/forthcoming therapies:* Guidance may evolve rapidly as trial data on inclisiran, new RNA drugs for TG and Lp(a), and others mature (Figure 2).

### The South Asian Phenotype: Well Represented in the Update

247 The South Asian phenotype of dyslipidemia is characterized by a  
248 unique and distinct lipid profile contributing to their high risk of pre-  
249 mature coronary heart disease (CHD). Key features include elevated  
250 triglycerides, low levels of high-density lipoprotein cholesterol (HDL-  
251 C), elevated lipoprotein(a) Lp(a) levels, and a higher burden of ath-  
252 erogenic particles despite relatively normal low-density lipoprotein  
253 cholesterol (LDL-C) levels compared to other ethnic groups. HDL

## ESC 2025 Lipid Guidelines -Key Takeaways



**Figure 2.** Key innovations from the 2025 ESC lipid guidelines: expanded risk modifiers, novel therapies, and intensified management strategies in ASCVD prevention and acute coronary syndromes.

Abbreviations: hs-CRP = high sensitivity C-reactive protein; Lp(a) = lipoprotein(a); ACS = acute coronary syndrome, LDL-C = low-density lipoprotein cholesterol; HIV = human immunodeficiency virus; NAFLD = non-alcoholic fatty liver disease; LLT = lipid-lowering therapy.

**Table 2**  
Key comparison of 2019 versus 2025 ESC/EAS dyslipidemia guidelines

Topic/section	2019 ESC/EAS guidelines	2025 Focused update
CV risk estimation tool	SCORE (fatal CVD, age 40 to 70 years)	SCORE2 (fatal & non-fatal CVD, <70 years); SCORE2-OP (≥70 to 89 years)
Risk modifiers	Emphasis on cholesterol, limited imaging	Now includes CAC, subclinical atherosclerosis, more modifiers
LDL-C treatment goals	Risk-category based, same targets	Unchanged, but re-emphasized and matched with new risk tools
Initial pharmacotherapy choice	Statin first-line	Still statin first-line, but more focus on early/intensive approach
Non-statin agents	Ezetimibe, PCSK9 inhibitors	Adds bempedoic acid (broadly), evinacumab (homozygous FH)
ACS (Initial therapy)	Stepwise postdischarge	Early/intensive combination therapy at index hospitalization encouraged
Hypertriglyceridemia	Fibrates & statins; omega-3 ambiguous	High-dose icosapent ethyl in high/very high risk; Volanesorsen for FCS
Lp(a) Measurement	Measure once/lifetime, risk enhancer	Now a Class IIa risk modifier for >50 mg/dL (105 nmol/L)
HIV infection	Consider statin if high LDL/dyslipidemia	Statin recommended (any LDL-C, age ≥40, regardless of risk)
Cancer (cardiotoxicity risk)	Less specific	Statins should be considered for high/very high risk patients
Dietary supplements	Not generally recommended	Explicitly not recommended for ASCVD prevention

254 particles in South Asians tend to be smaller, dysfunctional, and pro-  
255 atherogenic.

256 The 2025 ESC/EAS lipid-focused update addresses the South Asian  
257 phenotype of dyslipidemia by recognizing the high cardiovascular  
258 risk associated with this ethnic group due to their unique lipid pro-  
259 file. South Asian ethnicity is explicitly mentioned as a high-risk factor  
260 in cardiovascular risk estimation algorithms like SCORE2.

261 *Key ways the ESC/EAS update addresses this include:*

- 262 • Classifying South Asians as a high-risk ethnic group with often  
263 lower LDL-C but a higher burden of atherogenic particles, such as  
264 small dense LDL and elevated lipoprotein(a). This justifies earlier  
265 and more intensive lipid-lowering therapy.
- 266 • Emphasizing LDL-C as the primary treatment target with recom-  
267 mended lower LDL-C goals in very high-risk groups, such as  
268 <55 mg/dL, which aligns with the need for aggressive manage-  
269 ment in populations like South Asians with premature cardiovas-  
270 cular disease.
- 271 • Supporting non-HDL cholesterol and apolipoprotein B as alterna-  
272 tive markers for risk assessment, particularly in patients with  
273 elevated triglycerides, a common feature in South Asians.
- 274 • Including recommendations for early risk screening and intensi-  
275 fied statin therapy, often combined with ezetimibe, especially in  
276 patients presenting with acute coronary syndromes.
- 277 • Highlighting the relevance of lipoprotein(a) testing in patients  
278 with a family history of premature cardiovascular disease,  
279 although with some caveats on routine testing depending on  
280 population and lab validation.
- 281 • Recognizing the coexistence of insulin resistance and diabetes in  
282 the lipid management approach, recommending aggressive  
283 statin treatment in diabetic patients, reflecting the higher preva-  
284 lence of diabetes in South Asians.

## 285 Conclusion

286 The 2025 ESC/EAS Focused Update implements substantial refine-  
287 ments in the management of lipid disorders, emphasizing individual-  
288 ized assessment of cardiovascular risk, evidence-based escalation of  
289 therapy, and the utilization of new pharmacological agents for chal-  
290 lenging scenarios. These rigorous, consensus-driven recommenda-  
291 tions set the contemporary benchmark for lipid management and  
292 ASCVD prevention in clinical practice (Table 2).

## 293 Rationale and Scope of the 2025 Update

294 The 2025 Focused Update of the European Society of Cardiology/  
295 European Atherosclerosis Society (ESC/EAS) Guidelines for the man-  
296 agement of lipid disorders introduces substantive advances in risk

297 assessment, therapeutic options, and evidence-based recommenda-  
298 tions, reflecting the evolving landscape of cardiovascular disease  
299 (CVD) prevention. This review synthesizes the core changes and con-  
300 textualizes them against the 2019 standard, with clinical implications  
301 for practice and research.



## 302 Declaration of competing interest

303 The authors declare that they have no known competing financial  
304 interests or personal relationships that could have appeared to influ-  
305 ence the work reported in this paper.

## 306 CRedit authorship contribution statement

307 **Akshyaya Pradhan:** Writing – original draft, Resources, Formal  
308 analysis, Data curation, Conceptualization. **Prashant Thandi:** Writing  
309 – original draft, Resources, Formal analysis, Data curation, Conceptu-  
310 alization. **Kunal Mahajan:** Writing – original draft, Resources, Con-  
311 ceptualization. **Ferdinando Iellamo:** Writing – original draft,  
312 Methodology, Formal analysis. **Pasquale Perrone-Filardi:** Writing –  
313 original draft, Formal analysis, Conceptualization. **Marco Alfonso**  
314 **Perrone:** Conceptualization.

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