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Similarities and differences between European and American guidelines on the management of blood lipids to reduce cardiovascular risk

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A B S T R A C T

The 2018 American Heart Association/American College of Cardiology/Multi-Society (AHA/ACC/MS) Guideline on the Management of Blood Cholesterol and the 2019 European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) Guidelines for the Management of Dyslipidemias: Lipid Modification to Reduce Cardiovascular Risk, that were recently released by the United States and Europe, provide new recommendations for the management of blood lipid levels based on the latest evidence. Despite many common points, there are several differences in the recommendations, including the definition of very-high-risk patient category, the recommendations for some categories of patients, such as those with diabetes, familial hypercholesterolemia, chronic kidney disease, and aged patients, and the use of ezetimibe and PCSK9 inhibitors. These differences suggest that multiple approaches can be used to manage lipid abnormalities in the context of cardiovascular risk reduction.

1. Introduction

The 2018 American Heart Association/American College of Cardiology/Multi-Society (AHA/ACC/MS) Guideline on the Management of Blood Cholesterol [1] and the 2019 European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) Guidelines for the Management of Dyslipidemias: Lipid Modification to Reduce Cardiovascular Risk [2] have been recently released by the United States and Europe, respectively, to provide new recommendations based on the latest evidence. These recommendations are primarily based on the largely recognized and unequivocal causal link between elevated levels of low density lipoprotein cholesterol (LDL-C) and atherosclerotic cardiovascular disease (ASCVD) [3], and the proof that any approach able to reduce circulating levels of LDL-C reduces ASCVD risk. These two guidelines share many common points, but there are also differences in the recommendations due to a different interpretation of the available evidence, that will be discussed in this review.

2. Comparing the guidelines: similarities and differences

The 2018 AHA/ACC/MS Guideline and the 2019 ESC/EAS Guidelines present several similarities, including the risk-based approach to determine intervention intensity, the use of patient history, clinical characteristics and laboratory data to identify individuals most likely to benefit from lipid-lowering therapy, who are categorized in four major groups (patients with clinical ASCVD, severe primary hypercholesterolemia, diabetes mellitus and primary prevention patients with high 10-year risk for ASCVD). Both recommend interventions based on the concept that patients having a higher baseline risk will have a greater absolute ASCVD risk reduction derived from the same reduction of LDL-C.

On the other hand, major differences are present and include the definition of risk categories, the risk calculation system, different LDL-C goals (as well as non-HDL-C and apoB goals in

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hypertriglyceridemic patients), a different use of atherosclerosis imaging tests, and use of pharmacotherapy that is based upon achieved LDL-C levels. Another major difference is that the ESC/EAS Guidelines do not distinguish people based on primary or secondary prevention, while for AHA/ACC/MS Guideline this distinction is maintained and based on the results of randomized controlled trials (RCTs). Furthermore, in their 2019 release, the ESC/EAS Guidelines have introduced relevant updates compared with the previous one, leading to the definition of new and lower LDL-C goals for high and very high-risk patients, and to the new concept of high-intensity lipid lowering (instead of high-intensity statin).

3. Major differences between the ESC/EAS Guidelines and the AHA/ACC/MS Guideline

Major differences between the European and the American guidelines concern the definition of very-high-risk patient category, the recommendations for patients with diabetes, familial hypercholesterolemia (FH), chronic kidney disease (CKD), and aged patients, as well as the use of ezetimibe and PCSK9 inhibitors.

3.1. Very-high risk patients

The two guidelines show differences in the categorization of very-high-risk patients (Table 1). Beside the different definitions used to classify a patient as very-high-risk, a major distinction is related to the pharmacological approach in this category, as the ESC/EAS Guidelines found their recommendation on the extrapolation of data showing that the absolute risk reduction is higher in patients with a higher baseline risk .

Although both guidelines recommend the use of high-intensity, or maximally-tolerated, statins as the first lipid-lowering approach, differences can be noted regarding the use of non-statin therapies, including ezetimibe and PCSK9 inhibitors. It should be also emphasized that ESC/EAS Guidelines suggest, for ASCVD patients who experience a second vascular event within two years, an LDL-C goal of <1 mmol/L (40 mg/dL) to be considered.

Older patients with ASCVD are differently approached by the two guidelines (Table 2): the AHA/ACC/MS Guideline suggests that in patients >75 years of age with ASCVD it is reasonable to initiate moderate- or high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, drug–drug interactions, patient frailty, and patient preferences; the ESC/EAS Guidelines recommend to treat older ASCVD (>age 65 years) patients as younger patients, and to start statin therapy in people aged >75 years if at high or very-high risk, with the indication to consider the presence of renal impairment or the potential for drug-drug interactions (starting with a low dose and titrated upward to achieve LDL-C treatment goals).

3.2. Diabetes

In both guidelines diabetes is recognized as a risk-conferring condition (Table 2); however, in the AHA/ACC/MS Guideline a moderate-intensity statin is recommended for all patients with diabetes, while a high intensity statin is considered reasonable for diabetic patients with multiple risk factors. Patients showing a ≥20% 10-year risk may be considered for high-intensity statins, or, if needed, ezetimibe to lower LDL-C by ≥ 50%. For diabetic patients >75 years of age, as well as for young patients (20–39 y) having long duration diabetes (≥10 years of type 2 diabetes mellitus, ≥20 years of type 1 diabetes mellitus) and evidence of end-organ involvement or an ankle brachial index <0.9, a weak recommendation is given for starting statin therapy.

In contrast, ESC/EAS Guidelines categorize diabetic patients as a moderate-, high- or very-high risk based on diabetes duration, number of concomitant risk factors, end-organ damage, and age of the patient. Patients presenting with target organ damage, at least 3 risk factors, or type 1 diabetes of >20 years duration are classified as very-high risk and an LDL-C goal of <1.4 mmol/L (55 mg/dL) is recommended. For those considered at high-risk (diabetes without target organ damage, duration <10 years, no additional risk factors), an LDL-C goal of <1.8 mmol/L (70 mg/dL), whereas an LDL-C <2.6 mmol/L (100 mg/dL) is recommended for diabetic patients at moderate-risk (type 1 diabetes in those aged <35 years, or type 2 diabetes in those aged <50 years, with duration of diabetes <10 years, and no evidence of target organ involvement). Statin therapy may be considered in both younger type 1 and type 2 diabetes patients (≤30 years of age) with evidence of end organ damage and/or an LDL-C level >2.5 mmol/L. However, in these patients, the measure of non-HDL-C and apoB rather than LDL-C may better unmask the dyslipidemic condition.

Table 1
Definition of Very-High Risk Category in the two Guidelines.

AHA/ACC/MS Guideline	ESC/EAS Guidelines
Major ASCVD Events • Recent ACS (within the past 12 mo) • History of MI (other than recent ACS event listed above) • History of ischemic stroke • Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation) **High-Risk Conditions** • Age ≥65 y • Heterozygous familial hypercholesterolemia • History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s) • Diabetes mellitus • Hypertension • CKD (eGFR 15–59 mL/min/1.73 m^2) • Current smoking • Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe • History of congestive HF	People with any of the following: • Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, 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 (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. • DM with target organ damage,a or at least three major risk factors, or early onset of T1DM of long duration (>20 years) • Severe CKD (eGFR <30 mL/min/1.73 m^2) • A calculated SCORE ≥10% for 10-year risk of fatal CVD • FH with ASCVD or with another major risk factor

ABI, ankle-brachial index; ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FH, familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; SCORE, Systematic Coronary Risk Estimation; T1DM, type 1 diabetes.

Table 2
Differences between ESC/EAS guidelines and AHA/ACC/multi-society guideline.

Category	ESC/EAS Guidelines	AHA/ACC/Multi-Society Guideline
	Recommendation (class of recommendation, level of evidence)	Recommendation (class of recommendation, level of evidence)
Diabetes	• In patients with T2DM at very-high risk, an LDL-C reduction of >_50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) is recommended (I, A) • In patients with T2DM at high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) is recommended (I, A) • Statins are recommended in patients with T1DM who are at high or very-high risk (I, A) • Intensification of statin therapy should be considered before the introduction of combination therapy (IIa, C) • If the goal is not reached, statin combination with ezetimibe should be considered (IIa B) • Statin therapy is not recommended in premenopausal patients with diabetes who are considering pregnancy or are not using adequate contraception (III, C) • Statin therapy may be considered in both T1DM and T2DM patients aged ≤30 years with evidence of end organ damage and/or an LDL-C level >2.5 mmol/L, as long as pregnancy is not being planned (IIb, C)	• In adults 40–75 years of age with diabetes mellitus, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated (I, A) • In adults 40–75 years of age with diabetes mellitus and an LDL-C level of 70–189 mg/dL (1.7–4.8 mmol/L), it is reasonable to assess the 10-year risk of a first ASCVD event by using the race and sex specific PCE to help stratify ASCVD risk (IIa B-NR) • In adults with diabetes mellitus who have multiple ASCVD risk factors, it is reasonable to prescribe high intensity statin therapy with the aim to reduce LDL-C levels by 50% or more (IIa B-R) • In adults older than 75 years of age with diabetes mellitus and who are already on statin therapy, it is reasonable to continue statin therapy (IIa B-NR)
Severe primary hypercholesterolemia	• People with markedly elevated single risk factors, in particular TC > 8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL) and patients with FH without other major risk factors are high-risk patients and LDL-C goals are a ≥50% reduction of LDL-C from baseline and an LDL-C <1.8 mmol/L (<70 mg/dL).: use maximally tolerated statin, and if necessary, ezetimibe to lower LDL-C to <1.8 mmol/L (70 mg/dL) • FH with ASCVD or another major risk factor are very-high risk patients: the goal is a ≥50% reduction from baseline and an LDL-C <1.4 mmol/L (55 mg/dL): if the goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended (I, C)	• In patients 20–75 years of age with an LDL-C level of ≥190 mg/dL (≥4.9 mmol/L) who achieve less than a 50% reduction in LDL-C while receiving maximally tolerated statin therapy and/or have an LDL-C level of ≥100 mg/dL or higher (≥2.6 mmol/L) ezetimibe therapy is reasonable (IIa, B-R) • In patients 20–75 years of age with a baseline LDL-C level ≥190 mg/dL (≥4.9 mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting TG ≤ 300 mg/dL (≤3.4 mmol/L) while taking maximally tolerated statin and ezetimibe therapy, the addition of a bile acid sequestrant may be considered (IIb, B-R) • In patients 30–75 years of age with heterozygous FH and with an LDL-C level of ≥100 mg/dL (≥2.6 mmol/L) while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered (IIb, B-R) • In patients 40–75 years of age with a baseline LDL-C level of ≥220 mg/dL (≥5.7 mmol/L) and who achieve an on-treatment LDL-C level of ≥130 mg/dL (≥3.4 mmol/L) while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered (IIb, C-LD)
Chronic kidney disease	• It is recommended that patients with Kidney Disease Outcomes Quality Initiative stage 3–5 CKD are considered to be at high or very-high risk of ASCVD (I, A) • The use of statins or statin/ezetimibe combination is recommended in patients with non-dialysis-dependent stage 3–5 CKD (I, A) • In patients already on statins, ezetimibe, or a statin/ezetimibe combination at the time of dialysis initiation, continuation of these drugs should be considered, particularly in patients with ASCVD (IIa, C) • In patients with dialysis-dependent CKD who are free of ASCVD, commencement of statin therapy is not recommended (III, A)	• In adults 40–75 years of age with LDL-C 70–189 mg/dL (1.7–4.8 mmol/L) who are at 10-year ASCVD risk of ≥7.5%, CKD not treated with dialysis or kidney transplantation is a risk-enhancing factor and initiation of a moderate-intensity statin or moderate-intensity statins combined with ezetimibe can be useful (IIa, B-R) • In adults with advanced kidney disease that requires dialysis treatment who are currently on LDL-lowering therapy with a statin, it may be reasonable to continue the statin (IIb, C-LD) • In adults with advanced kidney disease who require dialysis treatment, initiation of a statin is not recommended (III: No Benefit, B-R)
Issues specific to women	No specific recommendations	History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia is considered a risk-enhancing factor
Older patients	• Treatment with statins is recommended for older people (>65 y) with ASCVD in the same way as for younger patients (I, A) • Treatment with statins is recommended for primary prevention, according to the level of risk, in older people aged ≤75 years (I, A) • Initiation of statin treatment for primary prevention in older people aged >75 years may be considered, if at high-risk or above (IIb, B) • It is recommended that the statin is started at a low dose if there is significant renal impairment and/or the	In patients older than 75 years of age with clinical ASCVD, it is reasonable to initiate moderate- or high intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug–drug interactions, as well as patient frailty and patient preferences (IIa, B-R)

(*continued on next page*)

Table 2 (*continued*)

Category	ESC/EAS Guidelines	AHA/ACC/Multi-Society Guideline
	Recommendation (class of recommendation, level of evidence)	Recommendation (class of recommendation, level of evidence)
Hypertriglyceridemia	potential for drug interactions, and then titrated upwards to achieve LDL-C treatment goals (I, C) • Statin treatment is recommended as the first drug of choice to reduce CVD risk in high-risk individuals with hypertriglyceridaemia [TG levels >2.3 mmol/L (>200 mg/dL)] (I, B) • In high-risk (or above) patients with TG levels between 1.5 and 5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2_2 g/day) should be considered in combination with a statin (IIa, B) • In primary prevention patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins (IIb, B) • In high-risk patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins (IIb, C)	• In adults 40–75 years of age with severe hypertriglyceridemia (fasting triglycerides ≥500 mg/dL [≥5.6 mmol/L]) and ASCVD risk of ≥7.5%, it is reasonable to address reversible causes of high triglyceride and to initiate statin therapy (IIa, B-R) • In adults with severe hypertriglyceridemia (fasting triglycerides ‡500 mg/dL [≥5.7 mmol/L]), and especially fasting triglycerides ≥1000 mg/dL (11.3 mmol/L), it is reasonable to identify and address other causes of hypertriglyceridemia, and if triglycerides are persistently elevated or increasing, to further reduce triglycerides by implementation of a very low-fat diet, avoidance of refined carbohydrates and alcohol, consumption of omega-3 fatty acids, and, if necessary to prevent acute pancreatitis, fibrate therapy (IIa, B-NR)

ESC/EAS Guidelines. Class of recommendation: I, is recommended or is indicated; IIa, should be considered; IIb, may be considered; III, is not recommended. Level of evidence: A, data derived from multiple RCTs or meta-analyses; B, data derived from a single RCT or large non-randomized studies; C, consensus opinion of the experts and/or small studies, retrospective studies, registries. **AHA/ACC/MS Guideline**. Class of recommendation: I, strong; IIa, moderate; IIb, weak; III: no benefit, benefit = risk; III: harm, risk > benefit. Level of evidence: A, high quality evidence from more than 1 RCT, meta-analyses of high quality RCTs, one or more RCTs corroborated by high-quality registry studies; B-R, moderate quality evidence from 1 or more RCTs, meta-analyses of moderate-quality RCTs; B-NR, moderate quality evidence from 1 or more nonrandomized studies, meta-analyses of such studies; C-LD, limited data, C-EO, expert opinion.

3.3. Severe primary hypercholesterolemia

A significant difference in the approach to patients with severe hypercholesterolemia has been observed between the two guidelines. In fact, the AHA/ACC/MS Guideline, despite recommending the use of maximally tolerated dose of statin and classifying as high-risk patients, provides different recommendation for patients who meet the diagnostic criteria for FH and those who do not: ezetimibe may be considered for those having an LDL-C ≥ 2.6 mmol/L (100 mg/dL), the addition of ezetimibe therapy is classified as reasonable and the addition of a PCSK9 inhibitor may be considered if the LDL-C level on statin plus ezetimibe remains ≥2.6 mmol/L (≥100 mg/dL) and the patient has multiple factors that increase the risk of ASCVD events. For patients with heterozygous FH with an LDL-C ≥ 2.6 mmol/L (≥100 mg/dL) on maximally tolerated statin and ezetimibe, a PCSK9 inhibitor may be considered.

In the ESC/EAS Guidelines, subjects with a total cholesterol >8 mmol/L (>310 mg/dL) or LDL-C >4.9 mmol/L (>190 mg/dL) are classified as high-risk, and maximally tolerated statin (plus ezetimibe, if required) is recommended to achieve an LDL-C goal <1.8 mmol/L (<70 mg/dL); patients with FH and ASCVD or another major risk factor are considered very-high-risk and an approach with maximally-tolerated statin and, eventually, ezetimibe is recommended. A PCSK9 inhibitor should be added if LDL-C remains ≥1.4 mmol/L (≥55 mg/dL) for those at very-high risk, and is reasonable for those at high risk with LDL-C above the goal (Table 2).

3.4. Primary prevention

The AHA/ACC/MS Guideline categorizes primary prevention patients as low risk (<5%), borderline risk (5%-<7.5%), intermediate risk (≥7.5%-<20%), and high risk (≥20%). For low risk patients, lifestyle changes are recommended to reduce risk factors; a moderate-intensity statin is recommended for borderline risk if risk enhancers are present, or for intermediate risk patients; a high-intensity statin is recommended only in high risk patients to reduce LDL-C by ≥ 50%. In the intermediate risk category, if uncertainty persists, the coronary calcium scoring (CAC) can be considered, to further stratify patients and provide information on the possible benefit of initiating statin therapy (CAC 1–99 favours statin initiation; with CAC ≥100 statin therapy must be initiated).

The ESC/EAS Guidelines categorize primary prevention patients as low- (having a 10-year calculated risk of fatal cardiovascular disease of <1%), moderate- (≥1 to <5%), and high-risk ≥5 to <10%; a very-high risk category has been introduced, having a 10-year calculated risk of fatal cardiovascular disease ≥10% using the SCORE risk calculator. The presence of any of a number of risk-modifying factors may be used to further stratify patients. For each category, a specific LDL-C treatment goal is defined (low: <3.0 mmol/L (116 mg/dL); moderate: <2.6 mmol/L (100 mg/dL); high risk: <1.8 mmol/L (70 mg/dL); and very-high risk: <1.4 mmol/L (55 mg/dL)). Also secondary goals based on the risk category are defined for non-HDL-C and apoB levels. The therapeutic approach includes statin therapy first, ezetimibe as add-on, and then PCSK9 inhibitors to achieve those goals (Table 2).

3.5. Chronic kidney disease

While CKD (eGFR 15–59 mL/min/1.73 m^2) is referred to as a risk-enhancing factor by the ACC/AHA/MS Guideline, the ESC/EAS Guidelines define very high-risk patients those with severe CKD (eGFR <30 mL/min/m^2) and high risk those with moderate CKD (eGFR 30–59 mL/min/1.73 m^2); in both cases guidelines recommend statin or intensification of statin (adding ezetimibe) in patients not on haemodialysis, while starting statin therapy in patients with dialysis-dependent CKD is not recommended (Table 2).

3.6. Women

ESC/EAS Guidelines do not differentiate recommendations between men and women, while the AHA/ACC/MS Guideline indicates premature menopause (<40 years of age) or pregnancy-associated preeclampsia as conditions that might increase ASCVD risk later in life, supporting statin initiation in borderline or intermediate risk patients (Table 2).

3.7. Hypertriglyceridemia

Different levels of plasma triglycerides are used to define hypertriglyceridemia (HTG), with AHA/ACC/MS Guideline indicating a fasting level ≥2 mmol/L (≥175 mg/dL), whereas the ESC/EAS Guidelines identifying a level of fasting TG of ≥1.7 mmol/(≥150 mg/dL) as being associated with increased ASCVD risk (Table 2). In HTG patients, especially in those presenting with TG ≥ 2.3 mmol/L (≥200 mg/dL), the AHA/ACC/MS Guideline indicates advantages in the measurement of apoB, which represents a risk-enhancing factor and favors initiation of statin therapy, or intensification in patients already taking a moderate-intensity statin. For patients with severe HTG (≥5.7 mmol/L, or ≥500 mg/dL) and an ASCVD risk ≥7.5%, it is reasonable to address reversible causes of HTG and to initiate statin therapy. Implementation of very low-fat diet and treatment with omega-3 fatty acids or, if needed, fibrates should be considered in patients with TG ≥11.3 mmol/L (≥1000 mg/dL) to reduce the risk of acute pancreatitis.

Along with exclusion of secondary causes and dietary intervention, statins are recommended as the first drug of choice in high-risk patients with TG > 2.3 mmol/L (>200 mg/dL), and fibrates may be considered in combination with statin in primary prevention patients or in high-risk patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL). The ESC/EAS Guidelines have also introduced the possibility to add icosapent ethyl 2 g twice daily in statin-treated, high-risk patients with TG levels between 1.5 and 5.6 mmol/L (135–499 mg/dL), based on the results of the REDUCE-IT trial, that were not available at the time of AHA/ACC/MS Guideline release [4].

3.8. Use of ezetimibe and PCSK9 inhibitors

The AHA/ACC/MS Guideline recommends that ezetimibe is used in very high-risk or high-risk patients who achieve <50% LDL-C reduction with maximally-tolerated statin therapy, while the ESC/EAS Guidelines recommend that it is used whenever LDL-C goals are not achieved on maximally tolerated statin therapy. Regarding PCSK9 inhibitors, the AHA/ACC/MS Guideline considers their use only in very-high risk ASCVD patients after maximally-tolerated statin and ezetimibe if achieve <50% reduction in LDL-C and have LDL-C > 1.8 mmol/L (>70 mg/dL), or patients with baseline LDL-C ≥4.9 mmol/L (≥190 mg/dL) after maximally-tolerated statin and ezetimibe showing an LDL-C reduction <50% and with LDL-C >2.6 mmol/L (>100 mg/dL). Conversely, the EAS/ESC Guidelines indicate the use of PCSK9 inhibitors in very-high risk or selected high-risk patients whose LDL-C is not at goal on maximally-tolerated statin therapy and ezetimibe.

4. Conclusions

Both European and American guidelines are centred on the established role of LDL-C-lowering as a key strategy to reduce the chance of having a CV event, despite some divergences in both the interpretation of the evidence and the consequent recommendations, and include different specific LDL-C goals and a different pharmacological approach to achieve them. On the other hand, both guidelines point on the relevant role of patient involvement to increase the compliance to the therapy, which may be critical when very expensive drugs are used, such as PCSK9 inhibitors, and that should be reserved only for very high CV risk patients. The different recommendations for guideline-based patient care also suggest that multiple approaches can be used to manage lipid abnormalities in the context of ASCVD risk reduction. Despite the great improvement in the management of dyslipidemias, gaps in the adherence to recommended treatments are still present and should be greatly faced up to further improve the prevention of ASCVD.

CRediT authorship contribution statement

Lale Tokgözoğlu: Conceptualization, Supervision. **Manuela Casula:** Supervision. **Angela Pirillo:** Writing - original draft, Writing - review & editing, Visualization. **Alberico L. Catapano:** Conceptualization, Supervision.

Declaration of competing interest

LT has received consulting fees/honoraria from Abbott, Amgen, Bayer, Daiichi-Sankyo, Jansen, MSD, Mylan, NovoNordisk, Pfizer, Recordati, Sanofi, Servier; MC and AP have nothing to disclose; ALC reports grants from Amgen, Sanofi, Regeneron personal fees from Merck, Sanofi, Regeneron, AstraZeneca, Amgen, Novartis, outside the submitted work.

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