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Primary and secondary cardiovascular prevention: Recent advances

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ABSTRACT

Cardiovascular disease (CVD) remains a leading cause of morbidity and mortality worldwide with 20 million deaths annually. Recent advances in both primary and secondary prevention strategies have shown promising results in reducing the incidence and recurrence of cardiovascular events, but a question of fundamental importance is whether we are effective enough when predicting risk only in those over 40 years of age and only for 10 years. A similarly important question concerns the pathophysiological border between primary and secondary prevention and whether we should reorient our focus to atherosclerosis prevention as a continuous process that becomes clinically apparent later in life.

The landscape of CVD prevention is rapidly evolving, with significant advancements in pharmacological treatments, technological innovations, and such lifestyle modifications as adopting a healthy diet, engaging in regular physical activity (PA), ensuring quality sleep, and

quitting smoking, being crucial in the prevention of coronary artery disease. Integrating these strategies into clinical practice can enhance the effectiveness of both primary and secondary prevention, ultimately reducing the global burden of cardiovascular disease.

This review highlights the latest developments and strategies aimed at diagnosis and preventing CVD. Key areas of focus include the use of novel agents and the role of digital health tools in improving both long-term patient adherence to evidence-based interventions and outcomes. The integration of these advancements into clinical practice has the potential to significantly enhance cardiovascular health and reduce the global burden of CVD.

Key words: atherosclerosis, cardiovascular disease, digital health, lipid-lowering agents, primary prevention, secondary prevention

INTRODUCTION

Cardiovascular disease (CVD) is a major public health concern, accounting for a significant proportion of deaths globally. Despite being largely preventable, CVD is responsible for over 20.5 million deaths annually [1, 2]. However, it is estimated that up to 90% of CVD cases can be prevented through the implementation of effective preventive measures [3]. Besides unmodifiable risk factors, such as older age, male sex, as well as genetic and racial background, there are also factors that can be directly modified [4]. Understanding and addressing the modifiable risk factors is crucial for developing effective prevention and management strategies. Atherosclerotic cardiovascular disease (ASCVD) is influenced by several modifiable risk factors, including blood apolipoprotein-B-containing lipoproteins [5–9], underweight and obesity [10, 11], high blood pressure [12], chronic renal disease [13], cigarette smoking [14], metabolic syndrome [15–17], and diabetes mellitus [18]. Coupled with appropriate diet and sleep health these components are a part of the Life's Essential 8 as defined by the American Heart Association [19]. Beyond the primary risk factors, there are numerous other relevant factors and clinical conditions that modify ASCVD risk. These include genetic predispositions [20], inflammatory mediators [21–23], oxidative stress [24–26], thrombotic tendency, and critically important lifestyle factors such as diet and PA [27]. There are also other factors that may influence cardiovascular risk, such as place of living (based on these there are different baseline CVD risks for different European nations) [28, 29]. A retrospective cohort study conducted in Catalonia, a low-risk region, revealed that European-born immigrants from high-

and very-high-risk countries exhibit a higher burden of coronary heart disease, hypertension, and obesity. These findings emphasize the necessity for early screening, individualized care plans, and adequate healthcare resource planning to address the unique health needs of this population and mitigate the risk of cardiovascular disease [28].

Prevention strategies are historically categorized into primary prevention, aimed at preventing the onset of CVD, and secondary prevention, focused on preventing both first and recurrent events in patients with established CVD. There are also two more categories: primordial and tertiary prevention, which: 1) address the prevention of developing risk factors and 2) decrease the risk for disability and loss of quality life years. This review discusses recent advances in both primary and secondary cardiovascular prevention, emphasizing pharmacological, lifestyle, and technological interventions.

RECENT ADVANCES IN PRIMARY PREVENTION

Development of risk assessment tools

The 2021 European Society of Cardiology (ESC) prevention guidelines introduced significant advancements in risk assessment tools, particularly with the development of the Systematic Coronary Risk Estimation 2 (SCORE2) and SCORE2-Older Persons (SCORE2-OP) [29]. Further refinements in risk assessment tools were introduced in the 2023 ESC guidelines with the addition of SCORE2-Diabetes [30]. These tools, which are finally using non-high-density lipoprotein cholesterol (instead of less predictive total cholesterol values), are designed to provide more accurate risk prediction for different age groups and European regions, enhancing the ability of healthcare providers to tailor preventive strategies effectively. Moreover, it allows for tailored preventive strategies that align with an individual's risk profile. The detailed risk estimates provided by these tools facilitate shared decision-making between patients and healthcare providers, ensuring that preventive measures align with the patient's preferences. More precise risk stratification can lead to better-targeted interventions, potentially reducing the incidence of cardiovascular events and improving overall patient outcomes. A few points, however, require further discussion. SCORE2 combined low and moderate cardiovascular risk into one group, which might lead to more patients requiring earlier pharmacotherapy to achieve more intensive targets (for example for low-density lipoprotein cholesterol [LDL-C] it is now one goal of 100 mg/dl/2.5 mmol/l). This algorithm also does not clearly prompt on how to evaluate the risk in those with well-recognized risk modifiers. Finally, SCORE2 only allows for risk stratification of those at age 40 or more and predicts the risk of cardiovascular evens and

mortality for only 10 years. For many patients (especially for those at low risk), the risk score may not be motivating enough for lifestyle changes and pharmacotherapy (if indicated). In addition, these scores do not differentiate the risk among those in very high-risk and extremely high risk groups, which is critically important in order to optimally prevent recurrent CVD events, heart failure, and mortality [31–33].

Systematic Coronary Risk Estimation 2 (SCORE2)

SCORE2 is an updated version of the original SCORE model, which estimates the 10-year risk of a first fatal and nonfatal (a difference with SCORE) ASCVD event [29]. The new model incorporates contemporary data and improves statistical methods to provide more precise risk estimates. One of the key features of SCORE2 is the inclusion of both fatal and non-fatal cardiovascular events, offering a more comprehensive risk assessment. Additionally, SCORE2 provides tailored risk predictions for individuals aged 40–69, allowing for more accurate stratification and management of cardiovascular risk. The model is also calibrated for different European regions, accounting for variations in cardiovascular disease incidence and mortality across countries [29].

SCORE2-Older Persons (SCORE2-OP)

SCORE2-OP is specifically designed for individuals aged 70 and older. This tool addresses the unique risk profiles and healthcare needs of older adults, who often have multiple comorbidities and a higher baseline risk of cardiovascular events. The model allows for the incorporation of factors that are particularly relevant to older adults, such as frailty and polypharmacy, to enhance risk prediction accuracy. SCORE2-OP aids clinicians in making informed decisions about preventive interventions, balancing the benefits and risks of treatment in older populations [29]. This model also has some weaknesses, including the fact that especially for high and very high-risk regions, all patients at the age of 70 years of age or more are in the very high-risk category.

SCORE2-Diabetes

This tool is designed to estimate the 10-year risk of both fatal and non-fatal cardiovascular events, including myocardial infarction (MI) and stroke, in individuals with type 2 diabetes mellitus (T2DM). By incorporating traditional cardiovascular risk factors — such as age, smoking, blood pressure, and cholesterol levels — alongside diabetes-specific markers like

HbA1c, age at T2DM diagnosis, and estimated glomerular filtration rate, SCORE2-Diabetes provides a more tailored and accurate risk prediction for patients aged 40–69 without ASCVD or severe organ damage [30]. Its integration into the ESC guidelines reflects a broader shift towards precision medicine in cardiovascular care, ensuring that patients with T2DM receive more individualized and evidence-based interventions to mitigate their elevated cardiovascular risk [30]. On the other hand, there is an ongoing discussion about whether or not we need calculators for every cardiovascular risk factor and/or condition that modifies this risk. Moreover, SCORE2 Diabetes may indicate that patients with type 2 diabetes may be at low to moderate risk what is not met in clinical practice, increasing the risk of therapy underutilization or using without enough intensity [34, 35].

Long-term/lifetime risk estimation

The problem that usually refers to low to moderate, and even high risk, is the fact that risk calculators usually indicate low numbers (e.g., <10%) depending on the age categories. This is one of the reasons that based on this score estimation, patients who do not clearly understand these numbers might be non-adherent to lifestyle changes and therapies, which in most situations are lifetime. Therefore, the new concept is to try to present risk not for the range of 10 years, but 30 years and longer, and preferably lifetime, to show for instance that being at the age of 42 years with the risk of 2% might mean that at the age of 65 years of age the risk is 25% if we do not improve our risk factors and will not be adherent to nonpharmacological and pharmacological therapies. One such approach was presented by the American Heart Association and it is called — the **PREVENT (Predicting Risk of Cardiovascular Disease EVENTs) risk algorithm** (https://professional.heart.org/en/guidelines-and-statements/prevent-calculator) [36]. This is a sex-specific, race-free model to predict risk of total cardiovascular disease (and components of ASCVD and heart failure [HF]) in adults 30 to 79 years of age. The prognostic performance of this risk model demonstrated good discrimination and calibration in the overall population and among various demographics and subgroups with obesity, T2DM, and chronic kidney disease. It is worth emphasizing that this model includes estimated glomerular filtration rate, and add-on models offer the flexibility to include additional measures of kidney (urine albumin-to-creatinine ratio), metabolic (hemoglobin A1c), and social (social deprivation index) risk determinants — a composite measure of area and level of based on 7 demographic characteristics used to quantify socio-economic variation in health outcomes [36, 37].

Another approach was suggested for individuals with elevated lipoprotein(a) (Lp[a]), as an independent risk modifier [38, 39]. Lp(a) is highly proatherogenic (6 × higher than LDL-C), prothrombotic (due to high homology with plasminogen [40, 41]), and proinflammatory (due to oxidised phospholipids that are covalently attached to kringle KIV10), and significantly re-stratifies CVD risk [39]. To make the whole picture easier and more practically it increases the calculated risk by one (low to moderate, moderate to high, etc.) [39]. Based on the European Atherosclerosis Society [38] and Polish guidelines [39] recommended **Lp(a) risk calculator** (https://www.lpaclinicalguidance.com), it is possible to estimate not only the lifetime CVD risk, but risk that is modified by the level of the lipoprotein(a). It is also very easy to see how treating modifiable risk factors (LDL-C, blood pressure, obesity, diabetes, smoking) diminishes this risk.

There are other risk algorithms, still not sufficiently validated, based on artificial intelligence approaches. One of them is a new risk score generated with machine-learning tools (AutoScore) based on data from family physicians' practices within the LIPIDOGRAM 2015 cohort study [25]. The **Lipidogram Risk Score** was based on data from 13 611 patients and analyzed the following risk factors: age, sex, BMI, alcohol consumption, smoking, presence of comorbidities — hypertension, diabetes mellitus, atrial fibrillation, chronic kidney disease, hypertension, history of MI, self-declared PA, place of residence and education level [42]. Each risk factor included in the model was given a certain number of points, which corresponded to its weighted importance in the model. The final risk score categories were defined by thresholds at 29, 38, and 46 points for low (<29), moderate (29–38), high (>38–46), and very high CVD risk groups (>46 points). The first score enables one to estimate the risk for adults >18 years of age with 5 years CVD risk prediction; soon an update with long-term risk prediction will be released [42] (Table 1).

IMPLEMENTATION OF NEW SCORES AND CLINICAL IMPACT

The new tools help clinicians categorize patients into risk groups, guiding decisions for preventive strategies. However, for certain populations, particularly those with extreme and complex risk profiles, these categories may be insufficient to capture the full scope of a given cardiovascular threat. In contrast, the Polish guidelines, which approved the International Lipid Expert Panel (ILEP) 2021 recommendations [43], go a step further by introducing an additional category — "extreme risk" [44]. This designation applies to individuals with conditions such as progressive cardiovascular disease (e.g. those after ACS with concomitant risk factors),

severe hypercholesterolemia (including familial hypercholesterolemia), or recurrent events despite optimal treatment. This definition was only slightly modified in the recent Polish diagnostic guidelines and the most recent ILEP recommendations 2024 [33, 45]. The introduction of this category emphasizes the need for even more aggressive lipid-lowering therapies (including upfront double or triple therapy) and cardiovascular management, recognizing the inadequacy of standard thresholds in addressing the nuances of extreme-risk patients. The Polish approach, by pushing beyond the ESC's stratifications, advocates for more tailored interventions for the most vulnerable patients [44].

The 2021 and 2023 ESC guidelines' introduction of SCORE2, SCORE2-OP and SCORE Diabetes marks a pivotal step forward in the prevention of ASCVD. However, the novel SCORE models are not fully applicable to individuals with genetic lipid disorders such as familial hypercholesterolemia, given the unique lipid profiles and cardiovascular risk patterns associated with these conditions. For such patients, specific LDL-C thresholds and treatment targets are recommended, irrespective of the calculated cardiovascular risk, to ensure optimal management of hypercholesterolemia and associated cardiovascular risk. This approach underscores the need for tailored therapeutic strategies in managing genetic lipid disorders, beyond generalized risk algorithms.

LIFESTYLE MODIFICATIONS

Lifestyle changes are a cornerstone of both primary and secondary prevention of ASCVD. These modifications include improvements in diet, increased PA, obtaining a sufficient quantity of good quality sleep, and smoking cessation, all of which are critical in reducing cardiovascular risk (46-49).

Optimal Diet

A healthy diet is fundamental to cardiovascular health (44,50,51). Mounting evidence recommends a diet rich in fruits, vegetables, whole grains, and lean proteins, while limiting the intake of saturated fats, trans fats, and sugars (52-54). Emphasis is placed on the Mediterranean diet, the DASH, low-fat, Nordic or Planetary Health one, which has been shown to reduce the risk of cardiovascular events (50-54). The Mediterranean diet includes high consumption of olive oil, nuts, seeds, and fish, which are sources of healthy fats (omega-3 fatty acids) and essential nutrients (50,55). Reducing dietary salt intake is also crucial, as it helps manage blood pressure, a significant risk factor for cardiovascular disease, but also the risk of direct damage of the endothelium and other direct effects affecting atherosclerosis progression risk (56).

Despite the fact that recommendations on the role of diet in the prevention of ASCVD remain largely unchanged, there are some new insights. Recent investigations emphasize the importance of a healthy diet as a whole, its quality (which seems to be even more important than dietary component quantity) rather than focusing on individual components. The recommendations highlight early implementation of healthy eating habits, nutritional education, the role of diet supplements, and nutraceuticals (with confirmed evidence based on efficacy [nutrivigilance] and safety) (29,52,57-60).

Physical activity

Scientific evidence supports the importance of PA in preventing cardiovascular diseases (CVD) and identifies specific types of exercise that yield beneficial outcomes [61, 62]. Regular physical activity, which is declared by 40% of people, but only <10% have every-day regular exercise, is another key component of lifestyle modification. The guidelines usually recommend at least 150 minutes of moderate-intensity aerobic exercise or 75 minutes of vigorous-intensity exercise per week, along with muscle-strengthening activities on two or more days per week [29, 61]. Physical activity helps improve cardiovascular fitness, reduce blood pressure, triglycerides, inflammation, oxidative stress, and manage weight. It also has beneficial effects on mental health, which can indirectly support cardiovascular health by reducing stress and promoting overall well-being.

The current approach is to convince patients to engage in types of exercise they enjoy the most in order to maintain long-term adherence to physical fitness. Notably, the role of step counting, which can be easily tracked using widely available smartwatches or phone apps, is now strongly emphasized [63, 64]. A recent meta-analysis revealed that taking a median of around 4000 steps per day can significantly reduce all-cause mortality. Additionally, each increase of 1000 steps per day is associated with a 15% reduction in all-cause mortality, and each increase of 500 steps may help reducing CVD mortality by 7%. The preferable number of steps per day is suggested to be between 6–13 000 depending on age, what can result in a 49% all-cause mortality reduction [65]. The “more the better” rule should be applied for this type of exercise; however, there is still inconsistent data on the average number of steps/day, and available data suggest a *plateau* effect for the number of steps over 16 000/day [65, 66].

Smoking cessation

Smoking is the 3rd most prevalent cardiovascular disease risk factor (after lipid disorders and hypertension) [67], and smoking cessation is one of the most effective measures for reducing CVD risk [68]. The importance of quitting smoking as a method of preventing cardiovascular diseases and the latest methods to achieve this are presented in the World Health Organization (WHO) guidelines, which were published in July 2024 [68]. Guidelines strongly advocate for comprehensive smoking cessation programs that include behavioural support and pharmacotherapy. The WHO endorses varenicline, bupropion, nicotine replacement therapy, and cytisine as effective pharmacotherapies supporting tobacco cessation. To enhance global access to these recommended medications, WHO launched a prequalification process for medicinal products targeting tobacco use disorders in 2023. Notably, in April 2024, Kenvue's nicotine gum and patch became the first nicotine replacement therapy products to receive WHO prequalification [68].

WHO also advocates for behavioural interventions, recommending routine brief counselling sessions (lasting 30 seconds to 3 minutes) by health workers in healthcare settings. For those seeking more comprehensive support, WHO suggests more intensive behavioural interventions, including individual, group, or phone counselling. Additionally, digital tools such as text messaging, smartphone applications, and internet programs are recommended as supplementary or self-management aids [68].

Quitting smoking can significantly lower the risk of MI, stroke, and other cardiovascular events. It is worth emphasizing that while talking about smoking, we should always think of all types of smoking, including e-cigarettes/electronic nicotine delivery systems, which is a great problem worldwide, significantly increasing CVD risk [14], and for many it is wrongly perceived as a method to quit smoking. Healthcare providers are encouraged to routinely assess smoking status and provide resources and support to help patients quit. The full utilization of the existing programs at the level of general practitioners should be also encouraged.

Good quality sleep

Recent advances in understanding the role of sleep in CVD prevention highlight the critical importance of maintaining high-quality sleep [69, 70]. Emerging research indicates that consistent, restorative sleep significantly reduces the risk of developing CVD by regulating blood pressure, reducing inflammation, and improving metabolic health [71, 72]. Based on the available data, it is suggested that for adults it is recommended to have 6–8 hours of sleep, indicating that both less and more might be associated with unfavourable health outcomes [29,

73]. Novel interventions aimed at enhancing sleep quality include cognitive-behavioural therapy for insomnia, which has shown promising results in improving sleep patterns and overall cardiovascular health [74]. Additionally, the integration of digital health technologies, such as sleep tracking apps and wearable devices, offers personalized insights and interventions to help individuals achieve better sleep hygiene. These innovations underscore the potential of sleep optimization as a vital component of primary CVD prevention strategies [75, 76] (Figure 1).

Role of mobile health (mHealth) technologies

The use of mobile health (mHealth) technologies is encouraged to support lifestyle modifications. mHealth tools, such as smartphone apps and wearable devices, can help individuals track their diet, physical activity, sleep quality, and smoking cessation progress. These technologies provide real-time feedback and personalized recommendations, enhancing patient engagement and adherence to lifestyle changes. mHealth tools can also facilitate communication between patients and healthcare providers, allowing physicians to have insight into numerous health parameters, and in the consequence enabling more timely interventions and support [46, 75–80] (Figure 2).

Technological innovations, particularly telemedicine and remote monitoring technologies, have become essential also in managing patients already with established ASCVD, and the rapid development of these methods was observed during the COVID-19 pandemic [81]. These tools enable continuous monitoring and timely intervention, significantly improving patient outcomes. Remote monitoring allows for the collection of vital health data, such as blood saturation, respiratory parameters, blood pressure, heart rate (and HR variability), and electrocardiograms, from patients in their own homes. This data can be transmitted to healthcare providers in real-time, facilitating early detection of potential issues and prompt medical intervention. Telemedicine has also expanded access to healthcare, allowing patients to receive consultations and follow-up care without the need for in-person visits. This is particularly beneficial for patients in remote or underserved areas. The integration of these technologies into routine care has shown to reduce hospital readmissions, improve medication adherence, and enhance overall disease management. As a result, remote monitoring and telemedicine are pivotal in the secondary prevention of CVD, helping to manage chronic conditions more effectively and prevent recurrent CVD events [82]. Healthcare providers

should enable more common access to remote monitoring tools with suitable reimbursement, if necessary.

ADVANCED IMAGING TECHNIQUES AND CVD RISK

Advanced imaging techniques have become increasingly important in the prevention and management of coronary artery disease. One of the most notable advancements is the use of **coronary artery calcium (CAC) scoring**. This non-invasive imaging technique utilizes coronary computed tomography angiography scans to detect and quantify calcium deposits in the coronary arteries. The presence and extent of these calcium deposits are strong indicators of atherosclerosis and atherosclerotic plaque and affect cardiovascular risk [83, 84]. By providing a detailed assessment of coronary artery calcification, CAC scoring allows for better risk stratification and more personalized treatment plans for patients (for statins and its intensity, combination therapy and upfront lipid-lowering therapies, aspirin application) [33, 40, 83–85]. It is worth emphasizing, however, that the CAC score does not replace risk stratification with the approved and recommended scores but can be an add-on parameter for optimal risk stratification in primary prevention patients at the risk [86].

In addition to CAC scoring, other advanced imaging techniques such as dual-energy CT and micro-CT have been emerged. These technologies offer enhanced imaging capabilities, allowing for more precise visualization of vascular calcifications and plaque characteristics [87]. Dual-energy CT, for instance, can differentiate between various tissue types and provide more accurate measurements of calcified and non-calcified plaque components. This level of detail is crucial for tailoring preventive and therapeutic strategies to individual patient needs. All these innovative methods allow even now (however it is still not a part of the recommendations) to assess not only plaque morphology with the assessment of the lipid core volume, but also the presence of soft atheroma plaque, and many other parameters, like total atheroma plaque volume, percent atheroma volume, law attenuation plaque, spotty calcifications and many others. The real predictive role of these parameters require final confirmation in well-designed large studies, because based on these results we will be able to offer patients the opportunity to optimally invest in their cardiovascular health as early as possible [88].

Furthermore, the integration of these advanced imaging techniques into clinical practice has facilitated the early detection of subclinical atherosclerosis, enabling timely intervention and potentially reducing (preventing or delaying) the incidence of adverse cardiovascular

events. By identifying high-risk patients who may benefit from more aggressive risk factor modification (nonpharmacological and pharmacological ones), healthcare providers can implement targeted therapies that improve patient outcomes and reduce the burden of ASCVD [83]. Overall, the advancements in imaging technology have significantly enhanced our ability to assess ASCVD risk and develop personalized treatment plans, ultimately contributing to better prevention and management of ASCVD.

CONCLUSIONS

In conclusion, the landscape of cardiovascular disease prevention is rapidly evolving, with significant advancements in risk stratification, imaging diagnostic methods, and both primary and secondary prevention strategies. The integration of lifestyle modifications, such as healthy dietary habits, regular physical activity, and smoking cessation, alongside innovative pharmacological treatments and technological innovations, has shown great promise in reducing the incidence and recurrence of cardiovascular events. It is, however, critical to note that when evaluating risk, we need to take into account not only the risk score result but also all risk modifiers. While treating we must not focus only on one risk factor (risk factors' silos: LDL-centric, glucocentric or obesity-centric approach), but always assume a comprehensive approach in order to minimize residual risk. Finally, even after optimal risk stratification, we need to avoid therapeutic inertia and nonadherence, as the latter might completely diminish our efforts [89–92]. The use of polypills [93], novel lipid-lowering agents, and digital health tools has enhanced patient adherence and outcomes, highlighting the importance of a comprehensive and personalized approach to cardiovascular care. As we continue to refine these strategies and incorporate new evidence-based practices, the potential to significantly reduce the global burden of ASCVD becomes increasingly attainable. Continued research and collaboration among healthcare providers, researchers, and patients are essential to further advance the field and improve cardiovascular health outcomes worldwide.

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Table 1. Comparison of selected available risk scoring algorithms, with strengths and weaknesses indications

RISK STRATIFICATION ALGORITHM	STRENGTHS	LIMITATIONS
Systematic Coronary Risk Estimation 2 (SCORE2)	• Applies non-HDL-C instead of TC what ensures better risk prediction • Estimates both fatal and nonfatal ASCVD events • Calibrated for males and females, different age groups and European regions at different CVD risk • Easy for application, repeatable • Online calculator available	• Only for individuals ≥40 years • Estimates only 10-year risk of a first fatal and nonfatal ASCVD event • Does not include multiple risk modifiers, what may result in risk underestimation • Combines low and moderate CVD risk groups into one, what might lead to earlier pharmacotherapy • Does not allow for extremely high-risk group evaluation
SCORE2-Older Persons (SCORE2-OP)	• Designed for individuals ≥70 years • Applies non-HDL-C instead of TC what ensures better risk prediction • Estimates both fatal and nonfatal ASCVD events • Calibrated for males and females, different age groups and European regions at different CVD risk • Easy for application, repeatable • Online calculator available	• Estimates only 10-year risk of a first fatal and nonfatal ASCVD event • Does not include multiple risk modifiers, what may result in risk underestimation • Does not allow for extremely high-risk group evaluation • For high and very high-risk regions, almost all patients are at very high-risk category
SCORE2-Diabetes	• Specifically designed to estimate the 10-year risk of both fatal and non-fatal cardiovascular events, including MI and stroke in T2DM patients • Calibrated for males and females, different age groups and European regions at different CVD risk • Includes diabetes-specific markers like HbA1c, age at T2DM diagnosis, and eGFR • Easy for application, repeatable • Online calculator available	• Only for individuals ≥40 years • Estimates only the 10-year risk of a first fatal and nonfatal ASCVD event • Does not include other recognized risk modifiers, what may result in risk underestimation • Combines low and moderate CVD risk groups into one, what might lead to earlier pharmacotherapy • Does not allow for extremely high-risk group evaluation • Enables diagnosis patients with T2DM at low to moderate what may result in inappropriate therapy intensity
Predicting Risk of Cardiovascular Disease EVENTs (PREVENT) risk algorithm	• For adults aged 30 to 79 years • Sex-specific, race-free model predicts risk of total cardiovascular disease (and	• Still unable stratifying the risk of individuals between 18 and 29 years of age • Lifetime risk cannot be calculated

	components of ASCVD and heart failure) • Calibrated for the overall population and among various demographics and subgroups with obesity, T2DM, and CKD • Includes lipid lowering and antihypertensive medication, eGFR, and additional measures of kidney (UACR), metabolic (HbA1c), and social (social deprivation index) • Easy for application, repeatable • Online calculator available	
Lp(a) risk calculator	• Estimates lifetime (up to 80 years of age) CVD risk • Calibrated for males and females • Estimates the risk modified by the Lp(a) level • Predicts risk of MI or stroke • Includes information on diabetes, CVD family history and antihypertensive therapy • Enables the evaluation of interventions related to the optimization of other modifiable risk factors to reduce the risk dependent on Lp(a) • Easy for application, repeatable • Online calculator available	• Still unable stratifying the risk of individuals between 18 and 29 years of age and ≥75 years • Does not allow for the risk prediction of aortic stenosis and other Lp(a)-specific outcomes • No information on LLT included • Does not include multiple risk modifiers, what may result in risk underestimation
LIPIDOGRAM Risk Score	• For all adults ≥18 years • Includes multiple CVD risk modifiers, including age, sex, BMI, alcohol consumption, smoking, presence of comorbidities - hypertension, T2DM, atrial fibrillation, MI history, self-declared physical activity, place of residence and education level • Easy for application	• Still requires validation • Now only offers 5-year risk prediction • Does not include well-recognized risk factors, like LDL-C/non-HDL-C or blood pressure levels • Does not allow for extremely high-risk evaluation • Online calculator unavailable

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; Hb1Ac, glycated hemoglobin/hemoglobin A1c; LDL-C, low density lipoprotein cholesterol; LLT, lipid lowering therapy; Lp(a), lipoprotein(a); MI, myocardial infarction; non-HDL, non-high-density lipoprotein; TC, total cholesterol; TD2M, type 2 diabetes mellitus; UACR, urine albumin-creatinine ratio

Figure 1. Comparison of different approaches to lifestyle changes that might help investing in cardiovascular health as early as possible and help preventing the first and recurrent CVD events and mortality. Based on [19, 77, 78]. The ILEP Simple Tips for the healthy heart based on unpublished data

Figure 2. Application of digital health technologies in cardiovascular medicine and prevention. Adopted from Verma et al. [80] (no permission required; License: Creative Commons Attribution [CC BY 4.0])