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# Editorial: The 2021 European Society of Cardiology (ESC) Guidelines on the Real-World Prevention of Atherosclerotic Cardiovascular Disease (ASCVD)

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**Abstract** Some of the most challenging guidelines for clinical practice include recommendations for disease prevention, which often involve lifestyle modifications, which may vary between populations. On August 30, 2021, the European Society of Cardiology (ESC) published new guidelines for primary and secondary prevention of atherosclerotic cardiovascular disease (ASCVD), endorsed by 12 European professional societies. Important features of the 2021 ESC guidelines include recommendations for disease prevention in individuals in clinical practice, including in older adults, with and without ASCVD, with diabetes, familial hypercholesterolemia, and chronic kidney disease (CKD). Importantly, and for the first time, the updated 2021 ESC guidelines also address the impact of environmental factors, including water, air, and soil pollution, on the risk of ASCVD. This Editorial aims to present and discuss how the latest 2021 ESC guidelines on the prevention of ASCVD have practical real-world applications in clinical practice.

**Keywords:** **Guidelines • Atherosclerosis • Cardiovascular Disease • Risk • Disease Prevention • Air Pollution • Editorial**

Clinical guidelines for the prevention, diagnosis and management of human disease are evidence-based and rely on the quality of clinical research, including data from randomized, controlled clinical trials (RCTs) [1]. When objective evidence is not available from clinical trials or population studies, a systematic review of the literature and meta-analysis of all currently available data contribute to clinical guidelines [2]. Because clinical and epidemiological data, diagnostic methods, treatments, and clinical trials continue to develop, clinical guidelines are regularly updated [1]. Some of the most challenging guidelines for clinical practice include recommendations for disease prevention, which often involve lifestyle modifications, which may vary between populations [3]. The most challenging of these guidelines involve recommendations for preventing atherosclerotic cardiovascular disease (ASCVD) [3]. Atherosclerosis has its origins in childhood and adolescence, long before the presentation of the clinical sequelae, which are varied and include ischemic heart disease (IHD), myocardial infarction (MI), cardiac dysrhythmia such as atrial fibrillation (AF), and stroke [3].

The European Society of Cardiology (ESC) provides consensus evidence-based guidelines for clinical practice that are regularly updated [4]. The ESC also maintains the EURObservational Research Programme (EORP), including international cardiovascular disease registries [5]. The aims of maintaining these clinical registries include evaluating clinical practice using quality indicators (QIs) and adherence to clinical guidelines [5]. Although the incidence and mortality rates from ASCVD are declining in many countries in Europe, it has a significant impact on public health [3]. The ESC Task Force has published regular clinical guidelines, including guidelines on cardiovascular disease prevention, which were published in 2016 [6]. It is now possible to estimate the risk of developing ASCVD in apparently healthy subjects, older individuals, and patients with established ASCVD [6]. Lifetime ASCVD risk estimates now replace 10-year risk algorithms and are available to support treatment decisions [7]. In patients older than 70 years, treatment decisions require a specific ASCVD risk score that takes account of competing non-ASCVD risk and specific treatments for low-density lipoprotein cholesterol (LDL-C) and blood pressure [7]. The ability to estimate individual risk of developing ASCVD has resulted in new guidelines from the ESC for ASCVD prevention in clinical practice [7].

On August 30, 2021, the ESC published new guidelines for primary and secondary prevention of ASCVD [7]. Twelve European professional societies have endorsed the 2021 ESC guidelines to guide physicians in managing healthy individuals and patients with established ASCVD, familial hypercholesterolemia,





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diabetes, and chronic kidney disease (CKD) [7]. The 2021 ESC guidelines add to the recommendations made in 2016 and include several updates that increase the real-world relevance and application of the recommendations [6,7]. These guidelines include recommendations on disease prevention aimed at primary care and hospital care and include a personalized treatment approach that provides for individual lifetime risk factors [7]. An important feature of the 2021 ESC guidelines is the attention to disease prevention in older adults, including individuals of 70 years and older [7]. These guidelines highlight the importance of assessing high-risk individuals by evaluating lifetime risk and gradually increasing treatment or lifestyle changes that reduce the risk of ASCVD [7]. The approach of clinical management 'stepwise intensification' is recommended to involve healthcare professionals and patients [7]. The new guidelines focus on disease risk factors, risk classification, and prevention of the clinical sequelae of ASCVD [7].

The 2021 ESC guidelines include updated risk-prediction algorithms for apparently healthy people, including the Systematic COronary Risk Evaluation (SCORE) 2 (SCORE2) model and the SCORE2-Older Persons (SCORE2-OP) model [7,8]. The 10-year ASCVD risk is estimated in apparently healthy people aged 40-69 years with SCORE2 and those aged ≥70 years with SCORE2-OP [7,8]. The SCORE2 and SCORE2-OP risk calculators are calibrated for European regional populations, based on the level of risk for ASCVD from the World Health Organization (WHO) [8,9]. The WHO low-risk countries for ASCVD include Belgium, Denmark, France, Israel, Luxembourg, the Netherlands, Norway, Spain, Switzerland, and the UK [9]. The WHO moderate-risk countries for ASCVD include Austria, Cyprus, Finland, Germany, Greece, Iceland, Ireland, Italy, Malta, Portugal, San Marino, Slovenia, and Sweden [9]. The WHO high-risk countries for ASCVD include Albania, Bosnia and Herzegovina, Croatia, the Czech Republic, Estonia, Hungary, Kazakhstan, Poland, Slovakia, and Turkey [9]. The WHO very high-risk countries for ASCVD include Algeria, Armenia, Azerbaijan, Belarus, Bulgaria, Egypt, Georgia, Kyrgyzstan, Latvia, Lebanon, Libya, Lithuania, Montenegro, Morocco, the Republic of Moldova, Romania, the Russian Federation, Serbia, Syria, Macedonia, Tunisia, Ukraine, and Uzbekistan [9].

The 2021 ESC guidelines aim to address the prevention of ASCVD in groups of patients in real-world clinical practice, with and without ASCVD, and with diabetes, familial hypercholesterolemia, and CKD [7]. These guidelines recommend that patients who require initial treatment undergo an evaluation of the 10-year ASCVD risk, followed by advice on lifetime risk, risk modifiers, treatment benefits, and consideration of patient preferences [7]. Further treatment is intensified after the first step if the patient has a high ASCVD risk profile [7]. General recommendations for all patients include lifestyle changes regarding diet, cessation of smoking, reduction of alcohol intake, and reduction of systolic blood pressure to less than 160 mmHg [7]. LDL-C targets are recommended based on age <50 years, age 50-69 years, and age ≥70 years, and the 10-year risk of ASCVD according to SCORE2 [7,8]. An LDL-C level at less than 100 mg/dL is recommended, which should be lower if the patient is at high risk for ASCVD [7,8]. Individuals under 50 years of age with a 10-year risk of ASCVD below 2.5% are low to moderate risk [7]. Individuals aged 50-60 years and 70 years and older with risk scores of <5% and <7.5% are in the low to moderate risk category for ASCVD [7]. However, individuals younger than 50 years, between 50-69 years, and age 70 years and older with a 10-year risk of ASCVD ≥7.5%, ≥10%, and ≥15%, are currently considered at high risk for ASCVD [7]. This age-associated stratification of risk differs from the 2016 ESC guidelines, which had thresholds of <5% (low or moderate risk), ≥5% to 10% (high risk), and ≥10% (very high risk) [6,7]. The lower risk threshold in younger people aims to avoid undertreatment to improve lifetime benefits [7].

The primary prevention recommendations of the 2021 ESC guidelines recommend using the selective cholesterol absorption inhibitor, ezetimibe, added to a statin if the LDL-C level is not adequately reduced [7]. A PCSK9 inhibitor is recommended as an addition if the LDL-C level is still not adequately reduced [7]. The 2021 ESC guidelines do not recommend aspirin for primary prevention in patients at low risk and moderate risk of ASCVD events due to the risk of bleeding [7]. Although the 2021 guidelines do not recommend routine genetic risk scores or the use of serum and urinary biomarkers, coronary artery calcium (CAC) scores may be used to improve risk classification for treatment decisions in primary prevention [7,10].

In the 2021 ESC guidelines, the recommendations for patients with established ASCVD are the same as in the 2016 guidelines for the treatment targets for LDL-C and systolic blood pressure [6,7]. Lifestyle changes and smoking cessation are recommended, with a target for systolic blood pressure of 130 to 140 mmHg and a target for LDL-C of less than 70 mg/dL [7]. The 2021 ESC guidelines recommend that high-risk ASCVD patients could benefit from treatment with colchicine (0.5 mg daily) as secondary prevention if other risk factors are not controlled [7]. The recommendation for colchicine is based on the recent COLCOT and LoDoCo2 clinical trials [11,12]. Patients at high risk for ASCVD with triglyceride levels >135 mg/dL are recommended to have treatment with icosapent ethyl, an omega-3 fatty acid formulation, in combination with a statin, based on findings from the REDUCE-IT clinical trial [13].

Importantly, and for the first time, the updated 2021 ESC guidelines also address the impact of environmental factors, including water, air, and soil pollution, on the risk of ASCVD [7]. Therefore, patients at high risk for ASCVD are advised to avoid long-term exposure to increased air pollution [7,14,15].





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## Conclusions

In considering the prevention of disease by assessing the lifetime risk of ASCVD in populations throughout Europe, the new 2021 ESC guidelines for primary and secondary prevention of ASCVD have implications for public health policy and individual responsibility for health in the context of increasing environmental concerns associated with air, soil, and water pollution [7,15].

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