# Cardiovascular Disease and Lifestyle Medicine

**Koushik R. Reddy, MD, FACC, FACLM, DipABLM**

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## INTRODUCTION

Despite numerous advances in our understanding of cardiovascular disease (CVD) pathophysiology, pharmacology, therapeutic procedures, and systems improvement, there hasn't been an expected decline in heart disease–related mortality in the United States since 2010.[1] Hypertension and diet-induced risk continue to be the leading causes of cardiovascular morbidity.[2] During the COVID-19 pandemic, for the year 2020, heart disease, a vastly preventable condition, remained the leading cause of death, outnumbering COVID-19-related deaths by 345,599.[3] Given the degree of disease burden, morbidity, and mortality, there is an urgent need to redirect our focus toward prevention and treatment through simple and cost-effective lifestyle strategies.[4]

## CURRENT BURDEN OF CARDIOVASCULAR RISK FACTORS

Over the course of the past century, heart disease has been the leading cause of death, except during the years of the flu pandemic of 1918-1920. During the first decade of the 21st century, annual age-adjusted decline in mortality rates for total CVD was around 5%. Starting around 2011, this trend in decline slowed down significantly, averaging <1% per year.[5] During the same period, deaths attributable to heart failure (HF) increased by 20%.[6,7] As per the American Heart Association's (AHA) 2021 Heart Disease and Stroke Statistics, the prevalence of cardiovascular risk factors among American youth ages 12 to 19 continues to be high: smoking, non-ideal body mass index (BMI), physical activity, cholesterol, blood pressure, and diabetes are at 4.3%, 36.7%, 74.6%, 22.8%, 18.8%, and 13.8%, respectively. Adherence with the AHA's Healthy Diet Score is listed as 0.0%.[8]

**Koushik R. Reddy, MD, FACC, FACLM, DipABLM**

AUTHOR AFFILIATION

Division of Cardiology, Department of Medicine, James A. Haley VA Medical Center and University of South Florida, Tampa, FL

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Given these trends, the AHA issued the Presidential Advisory on 2030 Impact Goals focusing on increasing health span and well-being through primordial, primary, and secondary preventive strategies.[9] Starting preventive and healthy lifestyle strategies early in life is the most effective and efficient way to accomplish the goals of expanding health span, while further expanding life span. Children and young adults provide a window of opportunity to promote health and prevent disease.[10-12] This review will outline the role of lifestyle in the development of CVD and review lifestyle modalities for the family physician to address in their care of patients at every stage of life and condition.

## GENETIC RISK OF CARDIOVASCULAR DISEASE AND LIFESTYLE

In the clinical practice of cardiovascular medicine, we often hear patients say, "Doc, the disease runs in my family." However, single-gene disorders are rare causes of CVD and related risk factors. Most of the genetic risk related to CVD is under the influence of a complex interplay between multiple genes and their expression. This is quantified by a polygenic risk score (PRS).[13] Among the UK Biobank participants, individuals with high cardiorespiratory fitness showed 43% lower risk of coronary heart disease (CHD), despite a high PRS.[14] From another analysis of the UK Biobank, it was noted that in the setting of high genetic risk, unfavorable lifestyle, compared to favorable lifestyle, increased the risk of stroke by 66%.[15] In an analysis of 3 prospective cohorts including 55,685 participants, it was noted that the 20% with highest PRS had a 90% higher risk of cardiac events. Interestingly, among individuals with a high PRS who conformed to healthy lifestyle, the risk of events was lowered by 46%. Based on these observations, healthy lifestyle significantly lowers event rates, even in the setting of high genetic risk.[16]

## STABLE CORONARY ARTERY DISEASE AND LIFESTYLE

The INTERHEART study demonstrated that nearly 90% of the population-attributable risk of myocardial infarction (MI)

across the world in both men and women is explained by 9 risk factors that are modifiable.[17] These include abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, lower consumption of fruits and vegetables, higher consumption of alcohol, and a lack of regular physical activity. In the 15-year follow-up of the COURAGE trial, which tested medical therapy versus revascularization in patients with stable ischemic heart disease, it was noted that the individuals with the highest number of controlled risk factors (smoking cessation, physical activity, proper nutrition, weight management, controlled blood pressure, and controlled low-density lipoprotein cholesterol [LDL-C]) had the lowest mortality.[18] However, adherence to healthy diet (whole grains, vegetables, fruits) continues to be very poor among patients with established CHD,[19] and a large percentage of patients with stable CHD continue to smoke.[20] Compliance with exercise, physical activity, and referral to cardiac rehabilitation among post-MI patients and patients with stable CHD continues to be poor.[21] Comprehensive lifestyle-centered programs as outlined in the Lifestyle Heart Trial and Mount Abu Open Heart Trial have shown benefits in terms of improved metabolic parameters, reduction in angina burden, and quality of life.[22,23] Similarly, in a meta-analysis of 14 randomized controlled trials (RCTs), structured lifestyle intervention in individuals with established coronary artery disease (CAD) has been shown to lower the relative risk of fatal cardiovascular events by 18%.[24]

## ATRIAL FIBRILLATION AND LIFESTYLE

Atrial fibrillation (AF) is the most common cardiac arrhythmia, and the lifetime risk of developing AF after age 55 is ~37%.[25] A vast majority of this burden is due to lifestyle-related factors and preventable comorbidities such as obesity, diabetes, hypertension, and obstructive sleep apnea.[25] Based on multiple observations, there is a strong association between obesity and AF.[26-29] In an age- and gender-adjusted meta-analysis of 51,646 participants from 7 cohort studies, estimates from Mendelian randomization were significant and consistent with a causal link between BMI and AF.[30] Weight loss of 10% or greater has been shown to significantly lower the burden of AF.[31-35] Similarly, regular exercise within the guideline-recommended levels has been shown to lower the burden of AF.[36-39] Interestingly, extremes of endurance exercise, achieved by <1% of the general population, have been shown to increase the risk of AF.[40-42] Mind-body practices such as yoga also have been shown to lower the burden of AF.[43] As outlined earlier, these risk factors and the related disease burden can be prevented and treated with healthy lifestyle strategies. Recently the American Heart Association issued its Scientific Statement on Lifestyle and Risk Factor Modification for Reduction of AF.[25]

## CONGESTIVE HEART FAILURE AND LIFESTYLE

The prevalence of HF continues to increase.[8] Most of the risk factors related to HF are preventable by healthy lifestyle choices.[44,45] In the Cardiovascular Health Study, it was noted that adherence to healthy lifestyle is associated with lower risk of developing HF.[46] Results from 2 large Swedish prospective cohorts showed that adherence to healthy lifestyle behaviors is associated with significantly lower risk of HF.[47,48] Similarly, data from the Physicians Health Study showed that adherence to healthy lifestyle is associated with significantly lower lifetime risk of HF.[49]

In a Finnish study of 18,346 men and 19,729 women with 14.1 years of mean follow-up, it was shown that compliance with all healthy lifestyle factors (abstaining from smoking, mainintaing a healthy BMI, regular physical activity, increased consumption of vegetables and fruits, and limiting alcohol consumption) was associated with significantly lower risk of HF.[50] Based on observational studies, obesity appears to be causally linked to HF.[51,52] It was noted in the Framingham Heart Study that for every 1-unit increase in BMI, the risk of HF goes up by 5% in men and 7% in women.[51] Similar observations are noted in subsequent recent studies.[53,54]

In the setting of existing HF, there is an obesity paradox, where higher BMI appears to be protective.[55] At this time there is not much evidence in support of weight loss and improved HF outcomes. However, weight loss helps with quality of life, symptom relief, and improvement of other comorbid conditions such as hypertension, diabetes, and obstructive sleep apnea.[54]

In an observational study with 19,485 participants and 127,110 person-years of follow-up, it was noted that poor cardiorespiratory fitness accounted for ~50% of HF risk.[56] In patients with HF, level of physical activity is a predictor of better prognosis, independent of BMI.[55,57]

Plant-based dietary patterns have been shown to play a key role in the prevention of cardiovascular risk factors.[58] In a population-based cohort of 32,921 men, it was noted that a Mediterranean dietary pattern lowers the risk of HF.[59] In a prospective analysis of 16,068 individuals over 8.7 years, it was noted that a plant-based dietary pattern lowers the risk of HF by 41% (hazard ratio [HR] 0.59; 95% confidence interval [CI]: 0.41-0.86; $P$=0.004).[60] In a meta-analysis of 2 small studies, it was noted that mindfulness practices such as yoga improved peak $VO_2$ and improved quality of life.[61] Mindfulness-based practices have been shown to improve symptoms in patients with established HF.[62] Lifestyle strategies should be an integral part of prevention and management of HF.

## PILLARS OF LIFESTYLE MEDICINE AND CARDIOVASCULAR DISEASE

The American College of Lifestyle Medicine defines lifestyle medicine as the use of evidence-based lifestyle therapeutic intervention—including a whole-food, plant-predominant eating pattern, regular physical activity, restorative sleep, stress management, avoidance of risky substances, and positive social connection—as a primary modality, delivered by clinicians trained and certified in this specialty, to prevent, treat, and often reverse chronic disease. Using these 6 pillars, the family physician is in an optimal position to educate, activate, and initiate a lifestyle-first approach with patients at risk for or with established heart disease. The evidence for these pillars is reviewed below.

### Nutrition

Diet-induced risk continues to be one of the leading causes of CVD and disability,[2] with suboptimal diet estimated to be responsible for 1 in 5 premature deaths worldwide.[63] High intake of dietary sodium and low intake of whole grains and fruits are the leading contributing factors.[64,65] In a recent analysis of the Framingham Cohort, it was noted that every additional daily serving of ultra-processed foods is associated with a 7% (95% CI: 1.03-1.12), 9% (95% CI: 1.04-1.15), 5% (95% CI: 1.02-1.08), and 9% (95% CI: 1.02-1.16) increase in the risk of hard CVD and CHD events, overall CVD, and CVD mortality, respectively.[66] Similarly, in a recent large prospective observational study, it was noted that the consumption of ultra-processed foods is associated with a significant increase in the risk of cardiovascular, coronary, and cerebrovascular disease.[67]

In a systematic review and meta-analysis of 30 RCTs, it was noted that the DASH diet (fruits, vegetables, nuts, seeds, legumes, low-fat dairy, and lean meats) significantly lowered systolic and diastolic blood pressure.[68] In another large meta-analysis and systematic review of RCTs, DASH showed the largest net effect of lowering systolic and diastolic blood pressure.[69] In a meta-analysis of 32 observational studies, it was noted that the consumption of vegetarian diets is associated with lower systolic and diastolic blood pressure.[70]

Accordingly, multiple US and international cardiovascular society guidelines support the DASH dietary pattern for the prevention and treatment of hypertension with class I indication and level of evidence A.[71,72] In a meta-analysis and systematic review, a vegetarian diet was associated with lower concentrations of total cholesterol (–29.2 and –12.5 mg/dL; $P<0.001$), LDL-C (–22.9 and –12.2 mg/dL; $P<0.001$), and high-density lipoprotein cholesterol (HDL-C) (–3.6 and –3.4 mg/dL; $P<0.001$).[73] In a systematic review and meta-analysis of RCTs, it was noted that vegetarian diets significantly and favorably lowered all lipid parameters, except triglycerides.[74] Similarly, in another systematic review and meta-analysis of controlled trials, a plant-based Portfolio dietary pattern rich in plant sterols and soluble fiber has been shown to lower LDL-C by 17%.[75]

Current clinical practice guidelines from multiple medical societies, in addition to evidence-based medical therapies, support a predominantly plant-based dietary pattern for lipid lowering.[76,77] Despite some limitations posed by epidemiology and the paucity of large, long-term RCTs, the overwhelming majority of nutritional research supports increasing the consumption of unprocessed plant-based foods. Consistent with the totality of available data, a plant-predominant dietary pattern is supported by the American College of Cardiology/American Heart Association (ACC/AHA)[76] and the US Department of Agriculture.[78] Within the spectrum of plant-based diets, it is important to make a distinction between the healthful and unhealthful plant-based diets. Compared to healthful plant-based diets, consumption of unhealthful processed plant-based diets is associated with higher risk of CHD.[79] Given that poor diet quality is now one of the leading risk factors, it is of paramount importance that diet screening be incorporated into every clinical encounter. Recently the AHA issued its Scientific Statement on Rapid Diet Assessment Screening Tools for Cardiovascular Disease Risk Reduction Across Healthcare Settings.[80] The American Society for Preventive Cardiology (ASPC) has recently outlined "Top 10 Dietary Strategies for Atherosclerotic Cardiovascular Risk Reduction" (**TABLE**).[81]

### Physical Activity

The 2018 Physical Activity Guidelines for Americans and the 2019 ACC/AHA CVD Primary Prevention Clinical Practice Guidelines recommend that adults accumulate at least 150 min/week of moderate-intensity or 75 min/week of vigorous-intensity aerobic activity (or an equivalent combination) and perform muscle-strengthening activities at least 2 days/week.[76,82] The US Centers for Disease Control and Prevention (CDC) Behavioral Risk Factor Surveillance System shows that the prevalence of physical inactivity (PI) between 2015 and 2018 was 31.7% for Hispanics, 30.3% for non-Hispanic Blacks, and 23.4% for non-Hispanic Whites.[83] About 75% of American youth ages 12 to 19 are not meeting ideal physical activity goals.[8] Sedentary behavior (SB) and PI are associated with increased mortality. PI accounts for 9% of premature deaths globally.[84]

In a systematic review and meta-analysis of 47 studies, it was noted that PI is associated with increased all-cause CVD incidence and CVD mortality.[85] The cardiovascular benefits of physical activity are mediated by antithrombotic, anti-

TABLE. **Top 10 dietary strategies for atherosclerotic cardiovascular risk reduction**[81]

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| 1. Incorporate nutrition screening into medical visits to assess dietary quality and determine need for referral to an RDN |
| 2. Refer patients to an RDN for medical nutrition therapy, when appropriate, for prevention of ASCVD |
| 3. Follow ACC/AHA Nutrition and Diet Recommendations for ASCVD Prevention and Management of Overweight/Obesity, Type 2 Diabetes (T2DM) and Hypertension |
| 4. Include NLA nutrition goals for optimizing LDL-C and non-HDL-C and reducing ASCVD risk |
| 5. Utilize evidence-based heart-healthy eating patterns for improving cardiometabolic risk factors, dyslipidemia and ASCVD risk |
| 6. Implement ACC/AHA/NLA nutrition and lifestyle recommendations for optimizing TG levels |
| 7. Understand the impact of saturated fats, trans fats, omega-3 and omega-6 polyunsaturated fats and monounsaturated fats on ASCVD risk |
| 8. Limit excessive intake of dietary cholesterol for those with dyslipidemia, diabetes and at risk for heart failure |
| 9. Include dietary adjuncts such as viscous fiber, plant sterols/stanols and probiotics |
| 10. Implement AHA/ACC and NLA physical activity recommendations for the optimization of lipids and prevention of ASCVD |

ACC, American College of Cardiology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; NLA, National Lipid Association; RDN, registered dietitian nutritionist; TG, triglycerides.

atherogenic, antiarrhythmic, and hemodynamic effects.[86,87] In addition, regular physical activity has been shown to offer psychological, emotional, and social benefits.[88,89] Physical activity has been shown to offer benefit for CVD risks such as hypertension,[90] hyperlipidemia,[91-93] and diabetes.[94] The overall cardiovascular benefits of physical activity are well established and are supported by a level I recommendation by the current ACC/AHA guidelines on primary prevention.[76] Similarly, exercise and physical activity have been shown to offer significant benefits in patients with established CAD[95,96] and HF.[97]

### Sleep

According to a consensus statement by the American Academy of Sleep Medicine and Sleep Research Society, 7 to 8 hours of sleep at night is considered ideal for optimal health.[98] According to the CDC, 35% of adults report sleeping less than 7 hours per night.[99] A systematic review and meta-analysis of prospective studies that included 474,684 participants showed that both short (<7 hours) and long (>9 hours) sleep durations are associated with an increased risk of CVD and mortality.[100] Similarly, in a recent dose-response meta-analysis, it was noted that deviation from the recommended 7 to 8 hours of sleep is associated with increased risk of CVD and mortality.[101]

In an analysis of 461,341 UK Biobank participants free of CVD, it was noted that short sleep duration (<6 hours) was associated with 20% higher adjusted risk (HR 1.20; 95% CI: 1.07-1.33) and longer sleep duration (>9 hours) was associated with 34% higher risk (HR 1.34; 95% CI: 1.13-1.58) of MI. These associations were independent of various sleep traits, and the Mendelian randomization was consistent with the causal relationship between sleep duration and MI.[102]

In an analysis of the MESA cohort, it was noted that sleep irregularity was associated with an increased risk of CVD, independent of traditional risk factors.[103] Based on these observations, a disturbed sleeping pattern appears to be a novel risk factor and causally linked to CVD. Given these implications, evaluation of sleep hygiene—in addition to screening for obstructive sleep apnea—should be a routine part of the scope of care for family physicians and cardiovascular specialists.[104]

### Stress and Emotional Well-being

Mental health is defined by the World Health Organization as "a state of well-being in which an individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community."[105] Components of positive psychology include positive emotions, sense of purpose/connection, gratitude, resilience, and happiness. Negative psychology, on the other hand, constitutes chronic stress, depression, anxiety, anger, hostility, negative emotion, and overall dissatisfaction. These psychological factors play a significant role in the development of cardiovascular disease.

In the INTERHEART study, it was noted that the population-attributable risk of developing MI was 35.7% and 32.5% from smoking and psychosocial factors respectively.[17] In addition, a meta-analysis of 118,696 participants from 6 studies noted that perceived stress from various sources increased the risk of CHD and related mortality by 27%.[106] A 2018 analysis of 151,144 participants from 9 studies has shown a 61% increased risk of CHD with post-traumatic stress disorder.[107] Acute bouts of anger/hostility and chronic anger have been linked to increased risk of CHD.[108,109]

In a recent meta-analysis of 2 cohorts from the Nurses' Health Study and Veterans Affairs Normative Aging Study, it was noted that after adjusting for other variables, women in the highest optimism quartile had a 14.9% longer life expectancy and a 35% reduction in cardiovascular events after adjusting for other variables.[110] Depression at baseline is associated with a 60% increased risk of all-cause mortality and 70% increased risk of MI.[111]

Treatment of psychological factors in the context of CVD prevention and treatment can be approached in many ways. The 2017 Scientific Statement on Meditation and Cardiovascular Risk Reduction by the AHA outlines the benefits and supports such practices.[112] It is important to screen for depression and stress in all patients, including those with established CVD, since early diagnosis and treatment will improve outcomes.[113] Simple tools such as the Patient Health Questionnaire-2 Depression Screen are very useful.[114] The 2021 Statement on Psychological Health, Well-Being, and the Mind-Heart-Body Connection by the AHA is a very useful resource for primary care physicians.[115]

## Substance Misuse

**Smoking.** Over the course of the past 50 to 60 years, due to public health policy and anti-tobacco campaigning, there has been a significant decline in smoking. However, 20% of American adults and 4% of youth ages 12 to 19 are currently smoking.[8] It is estimated that tobacco smoke contains about 7000 toxic chemicals and 69 carcinogens.[116] These chemicals and toxins are implicated in CVD through various mechanisms such as changes in heart rate, blood pressure, inflammation, endothelial dysfunction, thrombosis, dyslipidemia, and autonomic dysregulation.[117]

All-cause mortality among male smokers ages 55 to 74 and female smokers ages 60 to 74 is at least 3 times higher than among those who never smoked.[118] Among patients with established CAD, smoking is associated with a marked increase in the risk of sudden cardiac death.[119] Smoking is associated with significantly increased odds of peripheral artery disease,[120] aortic aneurysms,[121] and stroke.[122] Similarly, smoking is associated with increased risk of AF and ventricular arrhythmias.[123,124] Secondhand smoke and the use of smokeless tobacco is associated with increased risk of CVD.[125,126]

**Alcohol.** According to the most recent data, around 85% of people over the age of 18 reported that they consumed alcohol at some point in time in their life. Close to 95,000 people die from alcohol-related disease every year in the United States.[127] In the United States, a standard drink contains roughly 14 grams of pure alcohol. This is equivalent to 12 ounces of regular beer (5% alcohol), 5 ounces of wine (12% alcohol), and 1.5 ounces of distilled spirits (40% alcohol).[128] Most medical society guidelines recommend limiting alcohol consumption to 2 drinks/day for men and 1 drink/day for women.[78] There may be some cardiovascular benefit to drinking within the recommended limits.[129] However, the most recent US dietary guidelines state that "Emerging evidence suggests that even drinking within the recommended limits may increase the overall risk of death from various causes, such as from several types of cancer and some forms of CVD. Alcohol has been found to increase risk for cancer, and for some types of cancer, the risk increases even at low levels of alcohol consumption (less than 1 drink in a day)."[78] In a recent analysis of 17,059 participants from the third National Health and Nutrition Examination Survey (NHANES III), the risk of stage 1 and 2 hypertension increased significantly in moderate drinkers (7-13 drinks/week) and heavy drinkers (≥14 drinks/week) when compared with individuals who never consumed alcohol.[130] Even the consumption of small amounts of alcohol has been shown to increase the risk of atrial fibrillation.[131]

Given the relationship between substance misuse and CVD, it is important that the use of tobacco and alcohol be discussed at every primary care visit. For successful achievement of tobacco cessation and maintenance, professional, individual, interpersonal, and community resources should be employed.

## Social Connection

Social support is best defined as "information leading the subject to believe that he is cared for and loved, esteemed, and a member of a network of mutual obligations."[132] Social isolation is often defined as the lack of social connection, and loneliness as the feeling of being alone, despite social connections.[133] The rates of social isolation and loneliness are increasing in the United States. As reported in the recent 2020 report by the National Academies of Sciences, Engineering, and Medicine, close to 30% of adults 45 and older are lonely and nearly 25% of adults over 65 are socially isolated.[134]

In a prospective analysis of 32,624 male healthcare professionals over 4 years, it was noted that poor social support was associated with a significantly increased risk of stroke and cardiovascular mortality.[135] It has been reported that established CHD, unmarried status, and the absence of a close confidant significantly increased the risk of mortality.[136] However, in a large RCT of patients with established CVD and MI, enhanced social support and cognitive behavioral therapy did not lower all-cause and cardiovascular mortality.[137] Screening for social isolation and loneliness is an important role of the family physician. The 2015 Scientific Statement by the AHA is a useful resource for primary care and cardiovas-

cular healthcare professionals to increase their awareness of social support and the role it plays in clinical outcomes.[138]

## SUMMARY

Progress to reduce CVD mortality has plateaued in the United States, and death and disability from CVD exceeded that from COVID-19 in 2020. There is an urgent unmet need to redirect our focus toward lifestyle to not only prevent but also treat CVD through effective lifestyle strategies. As outlined in this review, a vast majority of cardiovascular risk factors and established CVD can be approached through the 6 lifestyle pillars utilizing a lifestyle-first or lifestyle-plus pharmacologic and procedural treatment plan at both the family physician and cardiovascular specialty level. The American Academy of Family Physicians has outlined various practice tools for the successful incorporation and implementation of lifestyle medicine into family practice.[139] With constructive and cooperative partnership between the public, healthcare professionals, educational institutions, health insurance agencies, and policymakers, we must bring about this paradigm shift in the interest of individual and national health. ●

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