Contemporary Cardiology
Series Editor: Peter P. Toth

Nathan D. Wong
Ezra A. Amsterdam
Peter P. Toth *Editors*

ASPC Manual of Preventive Cardiology

Second Edition

ASPC

Humana Press

Contemporary Cardiology

Series Editor:

Peter P. Toth
Ciccarone Center for the Prevention of Cardiovascular Disease
John Hopkins University School of Medicine
Baltimore, MD
USA

For more than a decade, cardiologists have relied on the Contemporary Cardiology series to provide them with forefront medical references on all aspects of cardiology. Each title is carefully crafted by world-renown cardiologists who comprehensively cover the most important topics in this rapidly advancing field. With more than 75 titles in print covering everything from diabetes and cardiovascular disease to the management of acute coronary syndromes, the Contemporary Cardiology series has become the leading reference source for the practice of cardiac care.

More information about this series at http://www.springer.com/series/7677

Nathan D. Wong • Ezra A. Amsterdam
Peter P. Toth
Editors

ASPC Manual of Preventive Cardiology

Second Edition

Humana Press

Editors
Nathan D. Wong
Heart Disease Prevention Program
Division of Cardiology
University of California, Irvine
Irvine, CA
USA

Ezra A. Amsterdam
Division of Cardiovascular Medicine
University of California, Davis
Sacramento, CA
USA

Peter P. Toth
Cicarrone Center for the Prevention of
Cardiovascular Disease
John Hopkins University
School of Medicine
Baltimore, MD
USA

The first edition of this book was published with Demos MedicalWong, Nathan D., Amsterdam, Ezra A., Blumenthal, Roger S. (Eds.), ASPC Manual of Preventive Cardiology, 1/e Softcover (Demos, 9781936287864, 2015, 296 p., $90.00)

ISSN 2196-8969 ISSN 2196-8977 (electronic)
Contemporary Cardiology
ISBN 978-3-030-56278-6 ISBN 978-3-030-56279-3 (eBook)
https://doi.org/10.1007/978-3-030-56279-3

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword

It is a privilege, albeit a rather daunting one, to follow the great Thomas A. Pearson who wrote the foreword to the previous edition of the *ASPC Manual of Preventive Cardiology*. I would like to think of this as a symbol of increasing recognition that the approach to our greatest cause of death, atherosclerotic cardiovascular disease (ASCVD), should be global. As mortality from ASCVD has declined in the United States, it has risen in developing countries of the world. And even a decline in age-specific mortality may be misleading as deaths may be transferred to older age groups, incident non-fatal cases in younger persons will be missed, and advances in therapy will result in more persons living with ASCVD with consequent accumulating healthcare costs. We are also all concerned about our inability to contain the epidemic of obesity and the specter of unfit, overweight young adults dependent on a cocktail of medications to contain their risks—"chemical salvage" if you will.

Tom Pearson gave due credit to the great Jeremiah Stamler. I would also like to recollect what Geoffrey Rose [1] taught us—firstly, that most cases of ASCVD arise in people at only modestly increased risk, simply because they are far more numerous than high risk people; high-risk *individual*s gain most from preventive measures but a complementary population approach is needed if ASCVD is to be effectively contained. Secondly, "The primary determinants of disease are mainly economic and social, and therefore its remedies must also be economic and social. Medicine and politics cannot and should not be kept apart." It behoves those of us who try to lead in preventive cardiology to be advocates for not only our individual patients but for societal change as well.

Preventive cardiology faces many challenges. The busy healthcare professional is faced with a tsunami of clinical practice guidelines, many very detailed and dense. Many of us were not trained in such aspects as communications, behavior change, or nutrition. The medical system may be hostile to our efforts—we may be reimbursed for treating sick people but not for keeping people healthy. These aspects make the *ASPC Manual of Preventive Cardiology* singularly important, making core principles and key aspects of prevention accessible to the harassed healthcare professional and written by a star-studded cast of authors.

Can we also begin to glimpse the future of prevention? Risk estimation involves applying risk estimates derived from populations to individuals, a very uncertain process. There is much talk about 'personalised' risk estimation. Will genetics help us? It is likely that we have underestimated the impact of the polymorphisms that determine risk, because their effect on 5-year risk is small whereas the impact on true lifetime risk may be great [2]. Also, we will likely see a disentangling of direct genetic effects from indirect effects on lipids and blood pressure. In contrast, the endless quest for new risk factors has been rather disappointing after the effects of the "big three" of smoking, lipids, and blood pressure have been taken onto account.

There is much talk about fashionable topics such as "big data," machine learning, and artificial intelligence. But epidemiologists have always dealt in large numbers, and the harmonisation of data from disparate sources, while exciting, is still challenging. And new methods of data analytics are not inherently magical,- we still have to define clear and answerable questions.

Finally, have we physicians been too paternalistic, too controlling? It is logical and pleasing to see more patient involvement in Guidelines, more development of motivational interviewing skills, and an increase in the teaching of health maintenance skills from childhood on.

In conclusion, I warmly welcome the *ASPC Manual of Preventive Cardiology* as a lucid, comprehensive, and insightful contribution that belongs in the library of every healthcare provider who practices preventive cardiology. It is an indispensable companion for those devoted to state-of-the-art medical practice.

Trinity College, Dublin, Ireland Ian M. Graham, FRCPI, FESC, FTCD

References

1. Rose G. The strategy of preventive medicine. Oxford: Oxford University Press; 1992.
2. Ference BA, Graham I, Tokgozoglu L, Catapano A. The impact of lipids on cardiovascular health. JACC Health promotion series. J Am Coll Cardiol. 2018;72:1141–56.

Preface

Despite significant declines in cardiovascular disease mortality over much of the last half century, rates have begun to rise once again, and annual healthcare costs due to cardiovascular diseases in the United States approach one trillion dollars. Cardiovascular disease has become the leading cause of death in more and more developing countries worldwide, fueled largely by the obesity and diabetes epidemic, which is also driving increases in cardiovascular disease in the United States. While coronary heart disease has traditionally been the focus of preventive cardiology, more comprehensive approaches addressing prevention of peripheral vascular disease, stroke, heart failure, atrial fibrillation, as well as cardiovascular disease related comorbidities including diabetes and chronic kidney disease are needed. Moreover, management limited to traditional risk factors such as cholesterol, blood pressure, and smoking needs to be greatly expanded with the advent of newer therapies to reduce cardiovascular disease risk in diabetes, evidence of benefit from treating inflammation, as well as the role of genetic evaluation to target those most likely to respond to risk reducing therapies.

This new edition of the *American Society for Preventive Cardiology (ASPC) Manual of Preventive Cardiology* features significant updates from newer guidelines of the American College of Cardiology, American Heart Association, and other societies for cardiovascular risk assessment and risk factor management. In just the last 5 years, we have witnessed perhaps a generation of advances in the field of preventive cardiology that have been incorporated into this new edition. The advent of proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors has brought low density lipoprotein cholesterol to lower levels than ever before, in many cases below 20 mg/dL, further addressing the problem of "residual risk" in our high-risk patients. This occurred simultaneously with release of key trials of sodium-glucose transport protein 2 (SGLT-2) inhibitors and glucagon-like peptide 1 (GLP1) receptor agonists, the first diabetes therapies to show cardiovascular risk reduction benefits. Moreover, the first two trials to prove the link between inflammation and atherosclerosis and its clinical sequelae have leveraged novel mechanisms to reduce cardiovascular disease risk. The end of the last decade was then topped off by the

first fish oil therapy, icosapent ethyl, to further reduce risk for cardiovascular events beyond statin therapy in high-risk patients.

The contributors of the 29 chapters in this new edition are experts in their respective fields of preventive cardiology and, along with the editors, have dedicated their careers to advancing this field. While each chapter includes much relevant scientific discussion of the latest clinical trials and other research, the goal of the *ASPC Manual of Preventive Cardiology* is to address contemporary, practical therapeutic approaches that enhance the practice of preventive cardiology by the wide range of providers essential for its practice—ranging from lifestyle interventionists, such as dietitians and exercise physiologists, to nurses and nurse practitioners, pharmacists, primary care providers, and specialists including endocrinologists and cardiologists. Guidance is also provided for development of a preventive cardiology center that encompasses this range of healthcare providers essential for optimizing cardiovascular disease prevention in our communities.

It is hoped the *ASPC Manual of Preventive Cardiology* will serve as the authoritative and most up-to-date source of clinically relevant information for healthcare providers, scientists, and trainees in the United States and beyond who have an interest in or who have dedicated their careers to prevent cardiovascular disease in their patients and communities. Moreover, with the ASPC growing from a small group of academic physicians 35 years ago to a multidisciplinary membership of more than 1000 members today, the *ASPC Manual of Preventive Cardiology* is intended to serve an even larger audience of specialists dedicated to the field.

Irvine, CA, USA — Nathan D. Wong
Sacramento, CA, USA — Ezra A. Amsterdam
Baltimore, MD, USA — Peter P. Toth

Acknowledgements

This edition of the *ASPC Manual of Preventive Cardiology* is dedicated to:

Drs. William B. Kannel, Jeremiah Stamler, and Nanette Wenger, giants in the field.

Nathan D. Wong: to my wife Mia, son David and parents Donald and Mew Lun Wong

Ezra A. Amsterdam: to my wife, Beulah, and daughters, Elana Amsterdam and Dina Amsterdam

Peter P. Toth: to my most valued and influential teachers: Roger Waltemyer, Louis Bixby, Clarence Suelter, Denton A. Cooley, Paul Seifert, and Barbara Anne Gooding.

We also wish to acknowledge Mr. Michael D. Sova, managing editor, for his tireless efforts and attention to detail in helping to assemble this book.

Contents

Contributors

Sura Abbas, MD Division of Cardiovascular Medicine, University of California Davis Medical Center, Sacramento, CA, USA

Abdulhamied Alfaddagh, MD Department of Medicine, Johns Hopkins Ciccarone Center for the Prevention of Cardiovascular Disease, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Ayan Ali, BS Tulane University School of Medicine, New Orleans, LA, USA

Yasameen Alismail, MD Division of Cardiovascular Medicine, University of California Davis Medical Center, Sacramento, CA, USA

Matthew Allison, MD, MPH Family Medicine and Public Health, University of California San Diego, La Jolla, CA, USA

Jaime P. Almandoz, MD, MBA Weight Wellness Program, Division of Endocrinology, University of Texas Southwestern Medical Center, Dallas, TX, USA

Ezra A. Amsterdam, MD, FACC, FAHA Division of Cardiovascular Medicine, University of California, Davis, Sacramento, CA, USA

Bettina M. Beech, DrPH, MPH Department of Health Systems and Population Health Science, College of Medicine, University of Houston, Houston, TX, USA

Emelia J. Benjamin, MD, ScM National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham, Massachusetts & Sections of Cardiovascular Medicine and Preventive Medicine, Boston Medical Center, Boston University School of Medicine, Boston, MA, USA

Department of Epidemiology, Boston University School of Medicine, Boston, MA, USA

Jeffrey S. Berger, MD, MS Center for the Prevention of Cardiovascular Disease, New York University School of Medicine, New York, NY, USA

Roger S. Blumenthal, MD Department of Medicine, Johns Hopkins Ciccarone Center for the Prevention of Cardiovascular Disease, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Gerd Brunner, MS, PhD Penn State Heart and Vascular Institute, Pennsylvania State University College of Medicine, Hershey, PA, USA

Matthew J. Budoff, MD Department of Cardiology, Lundquist Institute at Harbor UCLA Medical Center, Torrance, CA, USA

Ewa Dembowski, MD Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Devinder S. Dhindsa, MD Department of Medicine (Cardiology Division), Emory University School of Medicine, Atlanta, GA, USA

Elizabeth H. Dineen, DO Susan Samueli Integrative Health Institute, University of California, Irvine, Irvine, CA, USA

Division of Cardiology, Department of Medicine, University of California, Irvine, Irvine, CA, USA

Melvin R. Echols, MD Department of Medicine, Division of Cardiology, Morehouse School of Medicine, Atlanta, GA, USA

Sergio Fazio, MD, PhD Center for Preventive Cardiology/Knight Cardiovascular Institute, Oregon Health & Science University, Portland, OR, USA

Keith C. Ferdinand, MD Department of Medicine, Tulane Heart and Vascular Institute, Tulane University School of Medicine, New Orleans, LA, USA

Barry A. Franklin, PhD Department of Cardiology (Cardiac Rehabilitation), Beaumont Health & Wellness Center, Royal Oak, MI, USA

Chellse Gazda, MD, MPH Weight Wellness Program, Division of Endocrinology, University of Texas Southwestern Medical Center, Dallas, TX, USA

Richard J. Glassock, MD Department of Medicine, Geffen School of Medicine at UCLA, Laguna Niguel, CA, USA

Scott M. Grundy, MD, PhD Center for Human Nutrition, University of Texas Southwestern Medical Center, Dallas, TX, USA

Martha Gulati, MD, MS, FACC, FAHA, FASPC Division of Cardiology, University of Arizona College of Medicine, Phoenix, AZ, USA

Yehuda Handelsman, MD, FACP, FNLA, FASPC, MACE Metabolic Institute of America, Tarzana, CA, USA

Aliza Hussain, MD Department of Medicine, Baylor College of Medicine, Houston, TX, USA

Nada El Husseini, MD, MHSc Department of Neurology, Duke University, Durham, NC, USA

Wayneho Kam, MD Department of Neurology, Duke University, Durham, NC, USA

Sadiya S. Khan, MD, MSc Division of Cardiology/Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Amit Khera, MD, MSc, FASCP Division of Cardiology, UT Southwestern Medical Center, Dallas, TX, USA

Arthur L. Klatsky, MD Department of Cardiology, Division of Research, Kaiser Permanente, Oakland, CA, USA

Jelena Kornej, MD, MSC National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham, Massachusetts & Sections of Cardiovascular Medicine and Preventive Medicine, Boston Medical Center, Boston University School of Medicine, Boston, MA, USA

Donald M. Lloyd-Jones, MD, ScM Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Hannah C. Lo, BS Division of Cardiovascular Medicine, University of California San Diego, La Jolla, CA, USA

Robin H. Lo, MD Internal Medicine, University of California at Irvine Medical Center, Irvine, CA, USA

Russell V. Luepker, MD, MS Division of Epidemiology and Community Health, University of Minnesota, Minneapolis, MN, USA

Muhammad Majid, MD Department of Cardiology, Division of Cardiovascular Medicine, University of California (Davis) Medical Center, Sacramento, CA, USA

Shaista Malik, MD, PhD, MPH Susan Samueli Integrative Health Institute, University of California, Irvine, Irvine, CA, USA

Division of Cardiology, Department of Medicine, University of California, Irvine, Irvine, CA, USA

Rina Mauricio, MD Department of Internal Medicine, Division of Cardiology, University of Texas Southwestern, Dallas, TX, USA

Anurag Mehta, MD Department of Medicine (Cardiology Division), Emory University School of Medicine, Atlanta, GA, USA

Vijay Nambi, MD, PhD Department of Medicine, Michael E DeBakey Veterans Affairs hospital and Baylor College of Medicine, Houston, TX, USA

Khurram Nasir, MD, MPH Division of Cardiovascular Prevention and Wellness Houston Methodist DeBakey Heart & Vascular Center, Center for Outcomes Research, Houston Methodist Hospital, Houston, TX, USA

Keith C. Norris, MD, PhD Department of Medicine, Division of General Internal Medicine and Health Services Research, David Geffen School of Medicine, University of California, Los Angeles, CA, USA

Afiachukwu Onuegbu, MD, MPH Department of Cardiology, Lundquist Institute at Harbor UCLA Medical Center, Torrance, CA, USA

Aryana Pazargadi, BS Division of Cardiovascular Medicine, University of California San Diego, La Jolla, CA, USA

Jamal S. Rana, MD, PhD Division of Cardiology, Kaiser Permanente Northern California, Oakland, CA, USA

Elsie Gyang Ross, MD, MSc Department of Surgery, Division of Vascular Surgery, Stanford University School of Medicine, Stanford, CA, USA

Alan Rozanski, MD Department of Cardiology, Mount Sinai Morningside Hospital and Mount Sinai Heart, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Anum Saeed, MD Heart and Vascular Institute, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Aparna Sajja, MD Department of Medicine, Johns Hopkins Ciccarone Center for the Prevention of Cardiovascular Disease, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Nazir Savji, MD Division of Cardiology, Johns Hopkins University, Baltimore, MD, USA

Douglas D. Schocken, MD Cardiology Division, Duke University School of Medicine, Durham, NC, USA

Michael D. Shapiro, DO, MCR Center for Prevention of Cardiovascular Disease, Fred M. Parrish Professor of Cardiology and Molecular Medicine, Winston-Salem, NC, USA

Stephen Sidney, MD, MPH Division of Research, Kaiser Permanente Northern California, Oakland, CA, USA

Geeta Sikand, MA, RD, FAND, CDE, CLS, FNLA Department of Medicine (Cardiology), University of California Irvine, Irvine, CA, USA

Laurence S. Sperling, MD, FACC, FACPFAHA, FASPC Department of Medicine (Cardiology Division), Emory University School of Medicine, Atlanta, GA, USA

R. Brandon Stacey, MD, MS Section in Cardiovascular Medicine, Wake Forest University School of Medicine, Winston-Salem, NC, USA

Neil J. Stone, MD Department of Medicine/Cardiology and Preventive Medicine, Northwestern Memorial Hospital/Feinberg School of Medicine, Winnetka, IL, USA

H. Robert Superko, MD, FASPC, FACC, FAHA Cholesterol, Genetics, and Heart Disease Institute, Carmel, CA, USA

Iwona Świątkiewicz, MD, PhD, FESC Division of Cardiovascular Medicine, University of California San Diego, La Jolla, CA, USA

Department of Cardiology and Internal Medicine, Nicolaus Copernicus University Collegium Medicum, Bydgoszcz, Poland

Nene Takahashi, MPH Western University of Health Sciences, College of Osteiopathic Medicine, Pomona, CA, USA

Pam Taub, MD Division of Cardiovascular Medicine, University of California San Diego, La Jolla, CA, USA

Peter P. Toth, MD, PhD Cicarrone Center for the Prevention of Cardiovascular Disease, John Hopkins University School of Medicine, Baltimore, MD, USA

H. Nicole Tran, MD, PhD Department of Internal Medicine, Kaiser Permanente Medical Center, Oakland, CA, USA

Jonathan T. Unkart, MD, MPH, MS Family Medicine and Public Health, Division of Preventive Medicine, University of California, San Diego, La Jolla, CA, USA

Sandhya Venugopal, MD, MS-HPEd Department of Internal Medicine, Division of Cardiovascular Medicine, University of California Davis Health, Sacramento, CA, USA

Nathan D. Wong, PhD, FACC, FAHA, FASPC, FNLA Heart Disease Prevention Program, Division of Cardiology, University of California, Irvine, Irvine, CA, USA

Focus on Cardiovascular Health Promotion and Disease Prevention: Opportunities for Improvement

Devinder S. Dhindsa, Anurag Mehta, and Laurence S. Sperling

Summary

- Prior reductions in cardiovascular mortality have seen stagnation and even a reversal in that trend despite modern and expensive technologies and therapies.
- This trend is due in part to an increase in the prevalence of obesity and diabetes, with resultant impact on other cardiovascular risk factors.
- The need for prevention is imperative and requires a comprehensive approach on a continuum of care from individual patients to large-scale public policy initiatives.

1 Introduction

The latter part of the twentieth century in the United States was notable for an unprecedented reduction in cardiovascular deaths. Importantly, most of the decrease in cardiovascular deaths, particularly between 1980 and 2000, was attributable to preventive efforts through improved awareness and treatment of traditional cardiovascular risk factors (smoking, dyslipidemia, hypertension, diabetes) [1]. Unfortunately, in recent years there has been stagnation in these gains with trends demonstrating a concerning increase in cardiovascular mortality, particularly in younger adults, due in part to a rise in obesity and diabetes in the United States [2–5]. Currently, there are 30 million Americans living with diabetes, 84 million with pre-diabetes, and 75 million with hypertension, and nearly 40% of Americans are obese [6, 7]. Disturbingly, the development of these cardiovascular risk factors

D. S. Dhindsa · A. Mehta · L. S. Sperling (✉)
Department of Medicine (Cardiology Division), Emory University School of Medicine, Atlanta, GA, USA
e-mail: lsperli@emory.edu

N. D. Wong et al. (eds.), *ASPC Manual of Preventive Cardiology*, Contemporary Cardiology, https://doi.org/10.1007/978-3-030-56279-3_1

is largely preventable. Our current healthcare system is inadequate in promoting healthy behaviors and incentivizes disease-focused care, often at advanced stages.

Despite outspending any other country with 18% of our gross domestic product on healthcare, the United States is ranked last among industrialized nations in healthcare value, measured as a composite of care process, access, efficiency, equity, and healthcare outcomes [8]. In 2016, cardiovascular disease spending was estimated at $555 billion [9]. By 2035, this cost is expected to increase to $1.1 trillion [10]. Although spending on technology for cardiovascular care had value in prior decades, the current trends in cardiovascular outcomes suggest this trend may no longer be true [5, 10–12]. As such, a greater focus on primordial and primary prevention is critical for the health and well-being of our communities and our future economy.

2 Defining Cardiovascular Health

A definition of cardiovascular health is useful for guiding efforts geared toward health promotion and disease prevention. In 2010, the Goals and Metrics Committee of the Strategic Planning Task Force of the American Heart Association (AHA) envisioned ideal cardiovascular health as a combination of three key factors: (1) absence of cardiovascular disease (CVD), (2) favorable levels of cardiovascular health factors, and (3) presence of favorable health behaviors [13]. The committee developed objective definitions for "ideal," "intermediate," and "poor" cardiovascular health based on these principles incorporating a combination of seven distinct cardiovascular risk factors and health behaviors [13]. These modifiable cardiovascular risk factors have been colloquially termed Life's Simple 7 and consist of blood pressure, total cholesterol, fasting blood glucose, smoking, physical activity, body mass index, and healthy diet (Table 1) [13]. Ideal cardiovascular health was defined as the presence of ideal levels of all seven metrics, intermediate cardiovascular health as the presence of at least one intermediate metric without any poor metrics, and poor cardiovascular health as the presence of at least one poor health metric [13].

Over the past decade, several studies have reported that individuals with ideal cardiovascular health are rare in American communities. The estimated prevalence of ideal cardiovascular health ranged from 0.5% to 12% in a systematic review conducted in 2016 [14]. A seminal investigation from the National Health and Nutrition Examination Survey (NHANES) revealed that the proportion of American adults meeting all seven ideal cardiovascular health metrics declined over time from 2.0% [95% CI, 1.5–2.5%] in 1988–1994 to 1.2% [95% CI, 0.8–1.9%] in 2005–2010 [15]. Women, non-Hispanic whites, and those with higher education levels were more likely to meet a greater number of these cardiovascular health metrics than their male, ethnic minority, and less educated counterparts. Furthermore, this investigation and several other epidemiologic studies have demonstrated the direct association of ideal cardiovascular health with favorable long-term cardiovascular outcomes [14, 15]. These findings illustrate the urgent need for cardiovascular health

Table 1 Modifiable risk factors and behaviors comprising the definitions of poor, intermediate, and ideal cardiovascular health

Metric	Poor	Intermediate	Ideal
Blood pressure	SBP ≥140 or DBP ≥90 mm Hg	SBP 120–139 or DBP 80–89 mm Hg or treated to goal	SBP <120 or DBP <80 mm Hg
Total cholesterol	≥240 mg/dl	200–239 mg/dl or treated to goal	<200 mg/dl
Fasting glucose	≥126 mg/dl	100–125 mg/dl or treated to goal	<100 mg/dl
Smoking status	Current smoker	Former smoker or quit ≤12 months ago	Never smoker or quit >12 months ago
Physical activity	None	1–149 min/week moderate intensity or 1–74 min/week vigorous intensity or 1–149 min/week moderate + vigorous intensity	≥150 min/week moderate intensity or ≥75 min/week vigorous intensity or ≥150 min/week moderate + vigorous intensity
Body mass index	≥30 kg/m^2	25–29.9 kg/m^2	<25 kg/m^2
Healthy diet score*	0–1 component	2–3 components	4–5 components

Adapted from American Heart Association's Life's Simple 7
*The Goals and Metrics Committee of the Strategic Planning Task Force selected five aspects of diet to define a healthy dietary score, which is detailed in their American Heart Association Special Report [13]
SBP systolic blood pressure, *DBP* diastolic blood pressure, *mm HG* millimeters of mercury, *mg/dl* milligrams per deciliter, *min* minutes, *kg/m^2* kilogram per meter squared

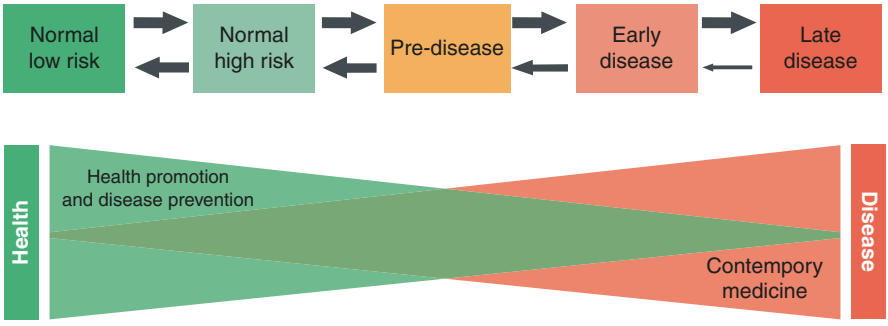

Fig. 1 The cardiovascular health/disease continuum. (Reprinted from Knapper et al. [16]. With permission from Elsevier)

promotion to help shift the cardiovascular health/disease continuum in favor of health (Fig. 1) [16].

A comprehensive, multifaceted approach that involves concerted efforts from key stakeholders is needed for promoting cardiovascular health. We will structure this chapter using the paradigm of the "three buckets of prevention": (1) traditional

clinical prevention, (2) innovative clinical prevention, and (3) community-wide prevention [17]. This framework is a useful means of approaching the continuum of prevention to discuss the challenges and opportunities related to cardiovascular prevention.

3 Bucket 1: Traditional Clinical Prevention

3.1 Improvement in Utilization and Adherence to Guideline-Recommended Therapies

Evidence-based guidelines are designed to guide clinicians and patients toward favorable outcomes for those with, or at risk for, atherosclerotic cardiovascular disease (ASCVD) [18, 19]. Unfortunately, current registries demonstrate inadequate uptake of recommendations, even those with a Class I indication. As an example, 28–36% of patients in the ACC National Cardiovascular Data Registry's (NCDR) Practice Innovation and Clinical Excellence (PINNACLE) Registry who were identified as high-risk benefit groups by current guidelines were not prescribed statins [20]. Additionally, other challenges include clinicians not prescribing the appropriate dose of statins despite supportive evidence for high-intensity statins in high-risk patients [21, 22]. In addition, there is significant lack of adherence among patients. In clinical trials and registries, nonadherence to statins is reported in up to 40% of subjects [23–26]. Together, between patient and clinician-related approaches to care, a large percentage of at-risk patients are not receiving guideline-directed medical therapy [27].

Importantly, lack of adherence poses both short-term and potential long-term risk. Younger patients accrue incremental benefit from early preventive therapy, yet are less likely to have hypertension diagnosed and treated, use statins as recommended, and are more likely to use tobacco [28–30]. Notably, in a high-risk secondary prevention cohort, 20% did not fill at least one of their prescribed cardiac medications within a month of hospital discharge after a myocardial infarction (MI), and of concern, nearly 50% of patients did not fill their antiplatelet therapy afterward [31]. Additionally, although lifestyle management remains the cornerstone of cardiovascular disease risk reduction, implementation remains a challenge, despite guideline recommendations. Americans have high rates of poor diet quality and physical inactivity [15, 28, 32]. Over one-fourth (28%) of US adults aged 35–64 are physically inactive, defined as never getting 10 min or more of leisure-time physical activity per day [28].

Multiple factors impact adherence. Out-of-pocket costs are a significant factor, although studies have shown that adherence does not improve substantially when medication copays are eliminated [33]. Additionally, clinicians and their patients, especially younger adults, may hesitate to start a medication regimen that could be lifelong, despite a strong indication to do so [34]. These challenges highlight multiple opportunities to address risk through better understanding and overcoming

barriers to adherence [23]. Whenever possible, clinicians should minimize patient cost, reduce barriers to obtaining medications, and simplify regimens [35]. Prescribing medication electronically reduces risk that a patient may lose a prescription. Pharmacy-initiated text reminders and automated refills are beneficial as well. Additionally, lower dosing frequency (i.e., utilizing long-acting formulations where possible) can improve adherence [36–38].

Evidence suggests that patients are more likely to make a lifestyle modification if their clinician recommends they do so [39]. One readily available lifestyle modification program is the National Diabetes Prevention Program, which enables people at risk for type 2 diabetes to participate in evidence-based lifestyle change programs that have shown significant long-term improvements on cardiovascular risk factors [40]. Registered dieticians, exercise physiologists, or promising community-based programs like Walk With a Doc should be utilized as well [41]. Engaging patients through involvement in shared decision-making, in which clinical guideline-based approaches in the context of individualized care, can strengthen therapeutic relationships, boosting patient engagement and medication adherence [42].

A systems approach to care, using protocols and electronic-medical record alerts, may be useful in overcoming some of the barriers on the part of physicians to implementation of guideline-directed therapy. Treatment protocols can help systematically identify patients who are eligible for intensification of clinical management, reduce variation between patients, simplify medication initiation and intensification, reinforce counselling on lifestyle modifications, and help in scheduling timely follow-up [34, 43]. Protocol implementation has been effective in improvement in performance on chronic disease quality indicators including hypertension control and may serve a critical role in cardiovascular risk reduction in our increasingly electronic and protocolized health system [44, 45].

3.2 Improving Utilization of Cardiac Rehabilitation

As a further example of challenges in implementation of guideline recommendations into clinical practice, cardiac rehabilitation (CR) remains significantly underutilized [46]. Cardiac rehabilitation (CR) services are an integral component in the care of patients with cardiovascular disease [47–49]. Referral to CR is a Class IA recommendation for secondary prevention established by the American Heart Association (AHA) and American College of Cardiology (ACC) after myocardial infarction (MI), percutaneous coronary intervention (PCI), or coronary artery bypass graft surgery (CABG), stable chronic heart failure, stable angina, cardiac transplantation, peripheral arterial disease, and cardiac valve surgery [50]. A meta-analysis of 34 randomized controlled trials showed that exercise-based CR programs in secondary prevention patients are associated with a lower risk of reinfarction (odds ratio [OR] 0.53; 95% confidence interval [CI] 0.38 to 0.76), cardiac mortality (OR 0.64; 95% CI 0.46 to 0.88), and all-cause mortality (OR 0.74, 95% CI 0.58 to 0.95), and CR also leads to improvements in cardiovascular risk

factors (i.e., lipid levels, blood pressure, tobacco use), as compared to usual care [51, 52]. Despite this, only about 60% of patients undergoing PCI are referred for cardiac rehabilitation [53] and even less enroll in CR. The safety and effectiveness of the traditional medically supervised, center-based CR is well established, but unfortunately CR remains substantially underused among eligible patients [54].

Data from several registries and databases indicate patient participation remains low across most demographic groups [49, 55]. Between 2007 and 2011, only 16.3% of Medicare patients and 10.3% of veterans participated in CR after hospitalization for MI, PCI, or CABG [55]. Improving referral rates through education and/or automatic generation of referrals following a hospitalization for a cardiac diagnosis is one possible solution to poor referral rates, but lack of access and other barriers including competing responsibilities, cost/financial viability, and perceived inconvenience for the patient require innovative solutions.

3.3 Improving Identification and Treatment of Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is the most common autosomal dominant genetic disorder, affecting one in 250 people worldwide in heterozygous form and approximately one in one million in homozygous form [56]. FH is caused by mutations in genes responsible for low-density lipoprotein (LDL) receptor and if left untreated places affected individuals at high risk for premature cardiovascular disease. FH is suggested to account for nearly 20% of myocardial infarctions before the age of 45, and the first presentation of the disease may be MI or sudden death, with homozygous FH resulting in significant ASCVD in childhood [57]. As such, early identification of this disease is critical, as starting therapy with statins and other lipid-lowering medications has been shown to attenuate this risk [58].

Despite the danger presented by this genetic disease, FH remains underdiagnosed and undertreated [59]. Public awareness and implementation of the recommendations from the World Health Organization regarding FH care have lagged substantially behind other advancements made within cardiovascular medicine [60]. Clinicians underestimate the prevalence, high level of risk, importance of treatment initiation within the first two decades of life, and the autosomal dominant inheritance pattern necessitating cascade family screening. Limited understanding by affected individuals of their disease process, economic ramifications of living with and affording lifelong care, and pragmatic concerns surrounding possible genetic discrimination pose additional barriers to care in those who are able to receive an accurate diagnosis [61]. Use of registries, such as the CASCADE FH Registry, and public awareness campaigns are critical to improving detection of this disease estimated to affect 34 million individuals worldwide [62]. Groups such as the FH Foundation have made significant progress in helping increase awareness and identify affected patients [63].

4 Bucket 2: Innovative Clinical Prevention

4.1 New Care Models

The prior discussion on the poor utilization of CR highlights the need for new care models in the modern era. Potential approaches include alternative site-, home-based, or hybrid models of CR, which can be carried out in the home or other non-clinical settings, alleviating access-related barriers for patients. European guidelines on CVD prevention state that "home-based rehabilitation with and without telemonitoring holds promise for increasing participation and supporting behavioral change" [63]. Comparisons of center-based CR and home-based CR show similar effects on quality of life and cost among patients with recent MI or PCI, with low rates of adverse events [49, 64, 65]. Theoretically, these types of programs can be used for other preventive strategies including management of risk factors, increasing physical activity, and maintenance of a healthy dietary pattern.

The increasing use of mobile technology serves as another opportunity to reduce gaps in access to CR through mobile health or "M-health" [66]. Mobile technology is widely utilized in the United States, with approximately 95% of adults owning a cellular device, and smartphone ownership estimated to be at 77%, an increase from 35% in 2011 [67]. This rise in smartphone adoption provides an opportunity to leverage advances in mobile technology, especially in capturing data regarding patient behaviors, physical activity, and enhanced two-way communication. Early research suggests "mCR" may be associated with greater utilization as post-MI patients assigned to a smartphone-based CR program had greater uptake (80% vs 62%), adherence (94% vs 68%), and completion (80% vs 47%) of a CR program compared to those assigned to traditional, center-based CR [68]. Both groups showed similar improvements in physiological and psychological outcomes suggesting equivalent benefits could be achieved with potential reductions in mortality and morbidity commensurate with those observed with center-based programs, with much greater reach [66].

Furthermore, the potential utility of m-health also extends to the promotion of healthy behavior modification beyond CR [69, 70]. A randomized controlled Tobacco, Exercise and Diet Messages (TEXT ME) trial showed that the use of lifestyle-focused text messaging resulted in significant reduction in low-density lipoprotein cholesterol, systolic blood pressure, body mass index, and smoking rates and an increase in physical activity compared to usual care in patients with established cardiovascular disease [71]. Patient education via social media and Internet sources has been shown to increase adherence in patients with non-cardiovascular conditions and could similarly impact cardiovascular care [5, 72, 73].

Systematic reviews indicate benefits of digital health interventions (telemedicine, web-based strategies, e-mail, mobile applications, text messages, remote monitoring) on improving cardiovascular risk [74]. An important area of future investigation will be exploring opportunities to optimize other emerging technologies (i.e., smartphone applications) to improve access, reach, and effectiveness of cardiovascular risk reduction strategies [66].

4.2 Improving Risk Assessment and Treatment of Cardiovascular Disease

Estimation of risk is the first step in cardiovascular disease prevention. In the 2018 ACC/AHA Cholesterol Guidelines, risk calculation guides initiation and intensity of therapy [75]. However, it is important for clinicians to recognize the limitations of population-based risk calculators for individual risk estimation. The 2018 Cholesterol Guideline recommends the identification of risk-enhancing factors beyond traditional cardiovascular risk factors and appropriate consideration of cardiac CT calcium scoring to reclassify risk with the goal of a more accurate and personalized assessment of risk (Table 2) [18]. Advances in genomics and biomarkers may enhance our ability to further assess risk facilitating tailored therapies. Polygenic risk scores may help identify patients at highest cardiovascular risk, even in the absence of traditional cardiovascular risk factors, who may benefit from earlier or more aggressive interventions [76, 77]. Large longitudinal studies, such as the NIH-funded *All of Us Research Program*, which is enrolling one million individuals, can collect the detailed genotypic and phenotypic data needed for this type of research [78]. Initiatives such as this will be invaluable in research and innovation moving forward to usher in an era of precision medicine with refined risk prediction and individualized targeted therapies.

4.3 Improving Partnerships and the Use of Registries

Registries offer clinicians and health systems the capability to evaluate real-world data to monitor practice patterns and trends. Use of the ACC's National Cardiac Data Registry (NCDR) and the Diabetes Collaborative Registry (tracking eight diabetes-related metrics and six either ACC/AHA-endorsed or Physician Quality

Table 2 Risk-enhancing factors in the 2018 ACC/AHA Cholesterol Guidelines

Family history of premature ASCVD (males <55 years; females <65 years)
Primary hypercholesterolemia (LDL-C 160–189 mg/dL; non-HDL-C 190–219 mg/dL)
Metabolic syndrome (three of the following: increased waist circumference, elevated triglycerides ≥150 mg/dL, elevated glucose, low HDL-C)
Chronic kidney disease
Chronic inflammatory conditions
*History of premature menopause (before 40 years) and history of pregnancy-associated conditions (*i.e., *preeclampsia)*
High-risk ethnicities (i.e., South Asian ancestry)
Elevated biomarkers (high-sensitivity C-reactive protein ≥2 mg/L; lipoprotein (a) ≥50 mg/dL or ≥ 125 nmol/L; apo B ≥130 mg/dL)
Ankle-brachial index < 0.9

Based on data from Ref. [75]
ASCVD atherosclerotic cardiovascular disease, *LDL-C* low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol, *apoB* apolipoprotein B

Reimbursement System (PQRS) measures) can increase awareness of gaps in care and may lead to improvements in reaching these quality metrics [79, 80]. Similarly, the CASCADE FH Registry provides similar data among FH patients with the goal of improving detection and care of FH patients [62].

5 Bucket 3: Community-Wide Prevention

5.1 Public Policy

Public policy and legislation are perhaps the most powerful tools that can help promote cardiovascular health on the local and national level [81]. A key set of public policies that have an outsized impact on cardiovascular health pertains to taxation of unhealthy consumables, particularly cigarettes [81]. Previous research has shown that higher cigarette taxes are associated with a decrease in consumption, especially among young individuals [82]. Simulation experiments suggest that a 40% tax-induced increase in cigarette prices would reduce smoking prevalence from 21% in 2004 to 15.2% in 2025 [83]. This change would translate into 13 million quality-adjusted life-years gained and $682 billion in total savings [83]. In addition to cigarette taxes, banning public smoking, improving access to healthy affordable foods, taxing sugar-sweetened beverage, restricting trans-fat use, and mandating calorie counts on chain restaurant menus are important public policy avenues that can help promote cardiovascular health.

5.2 Public Health Initiatives

Several public health initiatives geared toward promoting cardiovascular health are operational at the local and national level. Among these, Million Hearts®, a national initiative co-led by the Centers for Disease Control and Prevention (CDC) and the Centers for Medicare and Medicaid Services (CMS), is one of the most ambitious. The initiative has set a goal of preventing one million heart attacks and strokes within 5 years by focusing on a small set of priorities selected for their ability to reduce heart disease, stroke, and related conditions [84]. These priorities include (1) keeping people healthy by reducing daily sodium consumption, prevalence of tobacco use, and physical inactivity; (2) optimizing care by increasing appropriate aspirin use, blood pressure control, cholesterol management, smoking cessation, and cardiac rehabilitation use; and (3) focusing on priority populations such as African Americans with hypertension, people aged 35–64 years, patients with a history of heart attack or stroke, and patients with mental or substance use disorders that consume tobacco [85]. Other publicly focused initiatives like the Let's Move campaign, AHA Go Red for Women, and National Institutes of Health's Heart Truth are focused on promoting cardiovascular health in specific populations.

5.3 Mass Media Campaigns

Mass media campaigns have the ability of promoting cardiovascular health by impacting large population segments. Smoking cessation campaigns are perhaps the best studied and have been associated with increased quitting rates among smokers [86]. Additionally, the Stanford Heart Disease Prevention Program and the Minnesota Heart Health Program were two large studies conducted focused on preventing CVD [86]. The results of these studies suggest that media campaigns can not only promote physical activity and healthy diet but also help increase CVD awareness [86].

5.4 Environmental Interventions

Environmental interventions are important methods for promoting cardiovascular health because building designs and city plans can encourage and facilitate physical activity among residents [81]. For instance, the Task Force on Community Preventive Services has observed that creating or improving access to places where physical activity is feasible results in a 25% increase in the proportion of people who are physically active at least three times a week [87]. Physical activity can be fostered through innovative land use and community design interventions to make it safe and convenient to be physically active [88]. Places for physical activity can be created or developed using existing spaces through enhanced access via shared use agreements [89]. Designing a community to support physical activity through activity-friendly routes to everyday destinations is a critical intervention in a country where over one-fourth (28%) of US adults aged 35–64 state they are not engaging in even 10 min or more of leisure-time physical activity per day [28].

5.5 School-Based Interventions

Schools can play an instrumental role in promoting cardiovascular health at an early age, as nearly 55 million American children spend a majority of their time in schools [81]. The structured framework in schools can be leveraged to provide health education and encourage children to participate in healthy activities on a daily basis. The SPARK (Sports, Play, and Active Recreation for Kids) and CATCH (Coordinated Approach To Child Health) programs are prime examples of such school-based interventions [90, 91]. In addition to promoting physical health, these programs have been shown to improve academic performance and decrease disciplinary problems [92, 93]. The programs are generally cost-effective and lead to an overall improvement in school environment.

5.6 Workplace Interventions

Employee healthcare costs are an important cause of financial strain for employers and improving employee cardiovascular health serves as a significant financial incentive. Several workplace interventions such as smoke-free zones, healthy food and beverage options, worksite wellness programs, and treadmill workstations can be helpful for promoting cardiovascular health at the workplace [94].

6 Conclusion

Improvements in health promotion and disease prevention are critical to turning the tide of rising cardiovascular mortality. Although technological and therapeutic advancements will accelerate, relying on these alone will be inadequate without addressing the main drivers of ASCVD. Despite significant challenges, there is tremendous opportunity for preventive cardiologists and cardiovascular preventive specialists to be at the forefront of new care models, important partnerships, and initiatives. Integrated strategies that encompass each of the three buckets of prevention are essential to the health of individuals and communities and to reducing the burden of cardiovascular diseases on society.

Disclosures None for any of the co-authors.

Funding DSD and AM are supported by the Abraham J. & Phyllis Katz Foundation (Atlanta, GA).

References

1. Ford ES, Ajani UA, Croft JB, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980–2000. N Engl J Med. 2007;356(23):2388–98.
2. Ford ES, Capewell S. Coronary heart disease mortality among young adults in the U.S. from 1980 through 2002: concealed leveling of mortality rates. J Am Coll Cardiol. 2007;50(22):2128–32.
3. Vaughan AS, Ritchey MD, Hannan J, Kramer MR, Casper M. Widespread recent increases in county-level heart disease mortality across age groups. Ann Epidemiol. 2017;27(12):796–800.
4. Sidney S, Quesenberry CP Jr, Jaffe MG, et al. Recent trends in cardiovascular mortality in the United States and public health goals. JAMA Cardiol. 2016;1(5):594–9.
5. McClellan M, Brown N, Califf RM, Warner JJ. Call to action: urgent challenges in cardiovascular disease: a presidential advisory from the American Heart Association. Circulation. 2019;139(9):e44–54.
6. Centers for Disease Control and Prevention. National Diabetes Statistics Report. 2017.
7. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity among adults and youth: United States, 2015–2016. NCHS data brief, no 288. Hyattsville: National Center for Health Statistics; 2017.

8. Schneider E., Sarnak D., Squires D., Shah A., Doty MM. Mirror, mirror 2017: international comparison reflects flaws and opportunities for better U.S. Health Care. The Commonwealth Fund, July 2017. https://interactives.commonwealthfund.org/2017/july/mirror-mirror/.
9. American Heart Association, American Stroke Association. Cardiovascular disease: a costly burden for America (projections through 2035). Washington, DC: American Heart Association; 2017. https://healthmetrics.heart.org/wp-content/uploads/2017/10/Cardiovascular-Disease-A-Costly-Burden.pdf. Accessed Nov 2019.
10. Cutler DM, McClellan M. Is technological change in medicine worth it? Health Aff. 2001;20(5):11–29.
11. Cutler DM, McClellan M, Newhouse JP, Remler D. Are medical prices declining? Evidence from heart attack treatments*. Q J Econ. 1998;113(4):991–1024.
12. Cutler D, McClellan M, Newhouse J. The costs and benefits of intensive treatment for cardiovascular disease. National Bureau of Economic Research. 1998. https://www.nber.org/papers/w6514. Accessed Nov 2019.
13. Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic impact goal through 2020 and beyond. Circulation. 2010;121(4):586–613.
14. Younus A, Aneni EC, Spatz ES, et al. A systematic review of the prevalence and outcomes of ideal cardiovascular health in US and non-US populations. Mayo Clin Proc. 2016;91(5):649–70.
15. Yang Q, Cogswell ME, Flanders WD, et al. Trends in cardiovascular health metrics and associations with all-cause and CVD mortality among US adults. JAMA. 2012;307(12):1273–83.
16. Knapper JT, Ghasemzadeh N, Khayata M, et al. Time to change our focus: defining, promoting, and impacting cardiovascular population health. J Am Coll Cardiol. 2015;66(8):960–71.
17. Auerbach J. The 3 buckets of prevention. J Public Health Manag Pract. 2016;22:215–8.
18. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol. A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018;73(24):25709.
19. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease. J Am Coll Cardiol. 2019;74(10):26029.
20. Maddox TM, Borden WB, Tang F, et al. Implications of the 2013 ACC/AHA cholesterol guidelines for adults in contemporary cardiovascular practice: insights from the NCDR PINNACLE registry. J Am Coll Cardiol. 2014;64(21):2183–92.
21. Arnold SV, Spertus JA, Masoudi FA, et al. Beyond medication prescription as performance measures. Optimal secondary prevention medication dosing after acute myocardial infarction. J Am Coll Cardiol. 2013;62(19):1791–801.
22. Salami JA, Warraich H, Valero-Elizondo J, et al. National trends in statin use and expenditures in the US adult population from 2002 to 2013: insights from the medical expenditure panel survey. JAMA Cardiol. 2017;2(1):56–65.
23. Hirsh BJ, Smilowitz NR, Rosenson RS, Fuster V, Sperling LS. Utilization of and adherence to guideline-recommended lipid-lowering therapy after acute coronary syndrome: opportunities for improvement. J Am Coll Cardiol. 2015;66(2):184–92.
24. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med. 2015;372(25):2387–97.
25. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004;350(15):1495–504.
26. de Lemos JA, Blazing MA, Wiviott SD, et al. Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes phase Z of the A to Z trial. JAMA. 2004;292(11):1307–16.
27. Turin A, Pandit J, Stone NJ. Statins and nonadherence: should we RELATE better? J Cardiovasc Pharmacol Ther. 2015;20(5):447–56.
28. Wall HK, Ritchey MD, Gillespie C, Omura JD, Jamal A, George MG. Vital signs: prevalence of key cardiovascular disease risk factors for million hearts 2022 – United States, 2011-2016. MMWR Morb Mortal Wkly Rep. 2018;67(35):983–91.

29. Wang TW, Asman K, Gentzke AS, et al. Tobacco product use among adults — United States, 2017. MMWR Morb Mortal Wkly Rep. 2018;67:1225–32. https://doi.org/10.15585/mmwr.mm6744a2.
30. Johnson HM, Thorpe CT, Bartels CM, et al. Undiagnosed hypertension among young adults with regular primary care use. J Hypertens. 2014;32(1):65–74.
31. Jackevicius CA, Li P, Tu JV. Prevalence, predictors, and outcomes of primary nonadherence after acute myocardial infarction. Circulation. 2008;117(8):1028–36.
32. Healthy People 2020. Reduce the proportion of adults who engage in no leisure-time physical activity indicator. Accessed at https://www.healthypeople.gov/node/5052/data_details on Nov 2019.
33. Choudhry NK, Avorn J, Glynn RJ, et al. Full coverage for preventive medications after myocardial infarction. N Engl J Med. 2011;365(22):2088–97.
34. Ritchey MD, Wall HK, George MG, et al. US trends in premature heart disease mortality over the past 50 years: where do we go from here? Trends Cardiovasc Med. https://doi.org/10.1016/j.tcm.2019.09.005.
35. Guide to Community Preventive Services. Cardiovascular disease: reducing out-of-pocket costs for cardiovascular disease preventive services for patients with high blood pressure and high cholesterol. Accessed at https://www.thecommunityguide.org/findings/cardiovascular-disease-reducing-out-pocket-costs-cardiovascular-diseasepreventive services on Nov 2019.
36. Flack JM, Nasser SA. Benefits of once-daily therapies in the treatment of hypertension. Vasc Health Risk Manag. 2011;7:777–87.
37. Iskedjian M, Einarson TR, MacKeigan LD, et al. Relationship between daily dose frequency and adherence to antihypertensive pharmacotherapy: evidence from a meta-analysis. Clin Ther. 2002;24(2):302–16.
38. Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. Clin Ther. 2001;23(8):1296–310.
39. Yang K, Lee Y-S, Chasens ER. Outcomes of health care providers' recommendations for healthy lifestyle among U.S. adults with prediabetes. Metab Syndr Relat Disord. 2011;9(3):231–7.
40. Orchard TJ, Temprosa M, Barrett-Connor E, et al. Long-term effects of the Diabetes Prevention Program interventions on cardiovascular risk factors: a report from the DPP outcomes study. Diabetic Med J Br Diabetic Assoc. 2013;30(1):46–55.
41. Walk with a Doc. Accessed at https://walkwithadoc.org/ on Nov 2019.
42. Martin SS, Sperling LS, Blaha MJ, et al. Clinician-patient risk discussion for atherosclerotic cardiovascular disease prevention: importance to implementation of the 2013 ACC/AHA guidelines. J Am Coll Cardiol. 2015;65(13):1361–8.
43. Go AS, Bauman MA, Coleman King SM, et al. An effective approach to high blood pressure control: a science advisory from the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention. J Am Coll Cardiol. 2014;63(12):1230–8.
44. Jaffe MG, Young JD. The Kaiser Permanente Northern California story: improving hypertension control from 44% to 90% in 13 years (2000 to 2013). J Clin Hypertens (Greenwich). 2016;18(4):260–1.
45. Young A, Ritchey MD, George MG, Hannan J, Wright J. Characteristics of health care practices and systems that excel in hypertension control. Prev Chronic Dis. 2018;15:170497. https://doi.org/10.5888/pcd15.170497.
46. Ritchey MD, Maresh S, McNeely J, et al. Tracking cardiac rehabilitation participation and completion among medicare beneficiaries to inform the efforts of a national initiative. Circ Cardiovasc Qual Outcomes. 2020;13(1):e005902.
47. Dalal HM, Doherty P, Taylor RS. Cardiac rehabilitation. BMJ. 2015;351:h5000.
48. Wenger NK. Current status of cardiac rehabilitation. J Am Coll Cardiol. 2008;51(17):1619–31.
49. Thomas RJ, Beatty AL, Beckie TM, et al. Home-based cardiac rehabilitation: a scientific statement from the American Association of Cardiovascular and Pulmonary Rehabilitation, the American Heart Association, and the American College of Cardiology. J Cardiopulm Rehabil Prev. 2019;140(1):e69–89.

50. Drozda J, Messer JV, Spertus J, et al. ACCF/AHA/AMA–PCPI 2011 performance measures for adults with coronary artery disease and hypertension. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures and the American Medical Association–Physician Consortium for Performance Improvement. Circulation. 2011;58(3):316–36.
51. Lawler PR, Filion KB, Eisenberg MJ. Efficacy of exercise-based cardiac rehabilitation post–myocardial infarction: a systematic review and meta-analysis of randomized controlled trials. Am Heart J. 2011;162(4):571–584.e572.
52. Taylor RS, Brown A, Ebrahim S, et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. Am J Med. 2004;116(10):682–92.
53. Aragam KG, Dai D, Neely ML, et al. Gaps in referral to cardiac rehabilitation of patients undergoing percutaneous coronary intervention in the United States. J Am Coll Cardiol. 2015;65(19):2079–88.
54. Sandesara PB, Lambert CT, Gordon NF, et al. Cardiac rehabilitation and risk reduction: time to "rebrand and reinvigorate". J Am Coll Cardiol. 2015;65(4):389–95.
55. Beatty AL, Truong M, Schopfer DW, Shen H, Bachmann JM, Whooley MA. Geographic variation in cardiac rehabilitation participation in medicare and veterans affairs populations. Circulation. 2018;137(18):1899–908.
56. Goldstein JL, Hobbs HH, Brown MS. Familial hypercholesterolemia. In: Scriver CR, Beaudet AL, Sly WS, et al., editors. The metabolic and molecular bases of inherited disease. 8th ed. New York: McGraw-Hill; 2001. p. 2863–913.
57. Bouhairie VE, Goldberg AC. Familial hypercholesterolemia. Cardiol Clin. 2015;33(2):169–79.
58. Luirink IK, Wiegman A, Kusters DM, et al. 20-Year follow-up of statins in children with familial hypercholesterolemia. N Engl J Med. 2019;381(16):1547–56.
59. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease : consensus statement of the European Atherosclerosis Society. Eur Heart J. 2013;34(45):3478–90.
60. Programme WHOHG. Familial hypercholesterolaemia (FH): report of a second WHO consultation, Geneva, 4 September 1998. Geneva: World Health Organization; 1999.
61. Representatives of the Global Familial Hypercholesterolemia Community. Reducing the clinical and public health burden of familial hypercholesterolemia: a global call to action. JAMA Cardiol. 2020; https://doi.org/10.1001/jamacardio.2019.5173.
62. O'Brien EC, Roe MT, Fraulo ES, et al. Rationale and design of the familial hypercholesterolemia foundation CAscade SCreening for Awareness and DEtection of Familial Hypercholesterolemia registry. Am Heart J. 2014;167(3):342–349.e317.
63. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J. 2016;37(29):2315–81.
64. Buckingham SA, Taylor RS, Jolly K, et al. Home-based versus centre-based cardiac rehabilitation: abridged Cochrane systematic review and meta-analysis. Open Heart. 2016;3(2):e000463.
65. Dalal HM, Zawada A, Jolly K, Moxham T, Taylor RS. Home based versus centre based cardiac rehabilitation: cochrane systematic review and meta-analysis. BMJ. 2010;340:b5631.
66. Sandesara PB, Dhindsa D, Khambhati J, et al. Reconfiguring cardiac rehabilitation to achieve panvascular prevention: new care models for a new world. Can J Cardiol. 2018;34(10, Supplement 2):S231–9.
67. The World in 2014: ICT Facts and Figures. International Telecommunications Union. ITU: Statshot. 2014.
68. Varnfield M, Karunanithi M, Lee CK, et al. Smartphone-based home care model improved use of cardiac rehabilitation in postmyocardial infarction patients: results from a randomised controlled trial. Heart. 2014;100(22):1770–9.

69. Redfern J, Thiagalingam A, Jan S, et al. Development of a set of mobile phone text messages designed for prevention of recurrent cardiovascular events. Eur J Prev Cardiol. 2014;21:492–9.
70. Pfaeffli Dale L, Dobson R, Whittaker R, Maddison R. The effectiveness of mobile-health behaviour change interventions for cardiovascular disease self-management: a systematic review. Eur J Prev Cardiol. 2016;23:801–17.
71. Chow CK, Redfern J, Hillis GS, et al. Effect of lifestyle-focused text messaging on risk factor modification in patients with coronary heart disease: a randomized clinical trial. JAMA. 2015;314:1255–63.
72. Scalzi LV, Hollenbeak CS, Mascuilli E, Olsen N. Improvement of medication adherence in adolescents and young adults with SLE using web-based education with and without a social media intervention, a pilot study. Pediatr Rheumatol. 2018;16(1):18.
73. Gabarron E, Årsand E, Wynn R. Social media use in interventions for diabetes: rapid evidence-based review. J Med Internet Res. 2018;20(8):e10303. https://www.jmir.org/2018/8/e10303
74. Widmer RJ, Collins NM, Collins CS, West CP, Lerman LO, Lerman A. Digital health interventions for the prevention of cardiovascular disease: a systematic review and meta-analysis. Mayo Clin Proc. 2015;90(4):469–80.
75. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the Management of Blood Cholesterol. A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73(24):e285–350.
76. Khera AV, Chaffin M, Aragam KG, et al. Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations. Nat Genet. 2018;50(9):1219–24.
77. Inouye M, Abraham G, Nelson CP, et al. Genomic risk prediction of coronary artery disease in 480,000 adults: implications for primary prevention. J Am Coll Cardiol. 2018;72(16):1883–93.
78. All of Us Research Program Investigators, Denny JC, Rutter JL, Goldstein DB, Philippakis A, Smoller JW, Jenkins G, Dishman E. The "All of Us" Research Program. N Engl J Med. 2019;381(7):668–76.
79. Maddox TM, Song Y, Allen J, et al. Trends in U.S. ambulatory cardiovascular care 2013 to 2017. JACC review topic of the week. J Am Coll Cardiol. 2020;75(1):93–112.
80. Brindis RG, Fitzgerald S, Anderson HV, Shaw RE, Weintraub WS, Williams JF. The American College of Cardiology-National Cardiovascular Data Registry™ (ACC-NCDR™): building a national clinical data repository. J Am Coll Cardiol. 2001;37(8):2240–5.
81. Weintraub WS, Daniels SR, Burke LE, et al. Value of primordial and primary prevention for cardiovascular disease: a policy statement from the American Heart Association. Circulation. 2011;124(8):967–90.
82. Carpenter C, Cook PJ. Cigarette taxes and youth smoking: new evidence from national, state, and local youth risk behavior surveys. J Health Econ. 2008;27(2):287–99.
83. Ahmad S, Franz GA. Raising taxes to reduce smoking prevalence in the US: a simulation of the anticipated health and economic impacts. Public Health. 2008;122(1):3–10.
84. Frieden TR, Berwick DM. The "Million Hearts" initiative--preventing heart attacks and strokes. N Engl J Med. 2011;365(13):e27.
85. CDC, HHS. Million hearts. https://millionhearts.hhs.gov/.
86. Wakefield MA, Loken B, Hornik RC. Use of mass media campaigns to change health behaviour. Lancet. 2010;376(9748):1261–71.
87. Dishman RK, Oldenburg B, O'Neal H, Shephard RJ. Worksite physical activity interventions. Am J Prev Med. 1998;15(4):344–61.
88. Guide to Community Preventive Services. Physical activity: built environment approaches combining transportation system interventions with land use and environmental design. Accessed on https://www.thecommunityguide.org/findings/physical-activity-built-environment-approaches Nov 2019.
89. Guide to Community Preventive Services. Physical activity: creating or improving places for physical activity. Accessed at https://www.thecommunityguide.org/findings/physical-activity-creating-or- improving-places-physical-activity on Nov 2019.

90. Luepker RV, Perry CL, McKinlay SM, et al. Outcomes of a field trial to improve children's dietary patterns and physical activity. The Child and Adolescent Trial for Cardiovascular Health. CATCH collaborative group. JAMA. 1996;275(10):768–76.
91. Sallis JF, McKenzie TL, Alcaraz JE, Kolody B, Faucette N, Hovell MF. The effects of a 2-year physical education program (SPARK) on physical activity and fitness in elementary school students. Sports, play and active recreation for kids. Am J Public Health. 1997;87(8):1328–34.
92. Sallis JF, McKenzie TL, Kolody B, Lewis M, Marshall S, Rosengard P. Effects of health-related physical education on academic achievement: project SPARK. Res Q Exerc Sport. 1999;70(2):127–34.
93. Dowda M, James F, Sallis JF, McKenzie TL, Rosengard P, Kohl HW 3rd. Evaluating the sustainability of SPARK physical education: a case study of translating research into practice. Res Q Exerc Sport. 2005;76(1):11–9.
94. Kahn EB, Ramsey LT, Brownson RC, et al. The effectiveness of interventions to increase physical activity. A systematic review. Am J Prev Med. 2002;22(4 Suppl):73–107.

National and Global Trends of Cardiovascular Disease Mortality, Morbidity, and Risk

Sadiya S. Khan, Stephen Sidney, Donald M. Lloyd-Jones, and Jamal S. Rana

Summary

- Age-adjusted mortality rates demonstrate continued, but slower declines due to heart disease, a plateau related to stroke and diabetes, and persistent increases related to hypertension.
- Among cardiovascular disease subtypes, mortality rates due to heart failure have increased substantially, by a 38% increase in the number of deaths from 2011 to 2017.
- The aging population (≥65 years), which represents the vast majority of all cardiovascular deaths, is projected to increase by 44% between 2017 and 2030 and will likely contribute to a growing burden of cardiovascular mortality in the USA.
- Significant geographic heterogeneity exists in cardiovascular disease mortality rates with the highest age-adjusted mortality rates in the south and in rural counties.
- One in two American adults have some form of cardiovascular disease (coronary heart disease, heart failure, stroke, and hypertension) on the

S. S. Khan
Division of Cardiology/Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

S. Sidney
Division of Research, Kaiser Permanente Northern California, Oakland, CA, USA

D. M. Lloyd-Jones
Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

J. S. Rana (✉)
Division of Cardiology, Kaiser Permanente Northern California, Oakland, CA, USA
e-mail: jamal.s.rana@kp.org

N. D. Wong et al. (eds.), *ASPC Manual of Preventive Cardiology*,
Contemporary Cardiology, https://doi.org/10.1007/978-3-030-56279-3_2

basis of nationally representative data from the National Health and Nutrition Examination Survey 2013 to 2016 survey cycles.
- Maintaining better cardiovascular health to middle age is associated with substantially lower risk of developing subclinical or clinical cardiovascular disease or death, indicating important strategies for future prevention efforts.

1 Introduction

The burden of cardiovascular disease (CVD) is rising once again in the USA and worldwide [1, 2]. Nearly 50% of Americans have some form of CVD (coronary heart disease [CHD], heart failure [HF], stroke, and hypertension) with greater rates in non-Hispanic blacks and other disadvantaged populations [3]. When hypertension is excluded, prevalence of CVD is estimated to be 9.0% in the general population. One of the most remarkable and unprecedented public health successes in the last half century has been the dramatic and persistent decline in age-adjusted CVD death rates. Between 1970 and 2010, CVD death rates declined by >50% and CHD death rates declined by >75% [4]. This decline has been attributed to progress in prevention and significant advances in medical and surgical treatments for CVD [5]. Nonetheless, CVD remains the leading cause of US mortality today, and a large proportion of which is preventable (Fig. 1a) [6]. While mortality rates continued to decline after 2000 [7], contemporary data now demonstrate that HD mortality rates plateaued in 2011 (Fig. 1b) [1, 8, 9]. Furthermore, a trend reversal has been observed undoing decades of progress in HD prevention and management with increasing HD death rates in certain population subgroups, such as younger Americans [10]. Increases in midlife mortality, in large part due to CVD, have led to a decrease in life expectancy for the first time in decades [11, 12]. The economic burden of CVD events (CHD, HF, and stroke) related to morbidity and healthcare costs continues to soar, accounting for >6 million hospital discharges and annual direct US costs exceeding $320 billion currently and projected to exceed $800 billion annually by 2030, when >42% of American adults are expected to have some form of CVD [13–15]. Finally, major health disparities in CVD burden persist [13].

At present, it is unclear what factors are contributing to the observed flattening and upward trends observed in CVD death rates, although a number of possible explanations have been posited. We and others have speculated that the worsening trends could be related to the obesity epidemic and consequent adverse changes in risk factors finally becoming manifest in CVD death rates [16]; it could also be due to ceiling effect of gains realized from medical interventions to prevent death among those with acute CVD events. Finally, absolute CVD deaths have increased, in part, due to the aging population. Most likely, the causes are multifactorial and may differ for each sex-race group; and if current trends continue, strategic goals for lowering the burden of CVD set by the American Heart Association (AHA) [17, 18], the

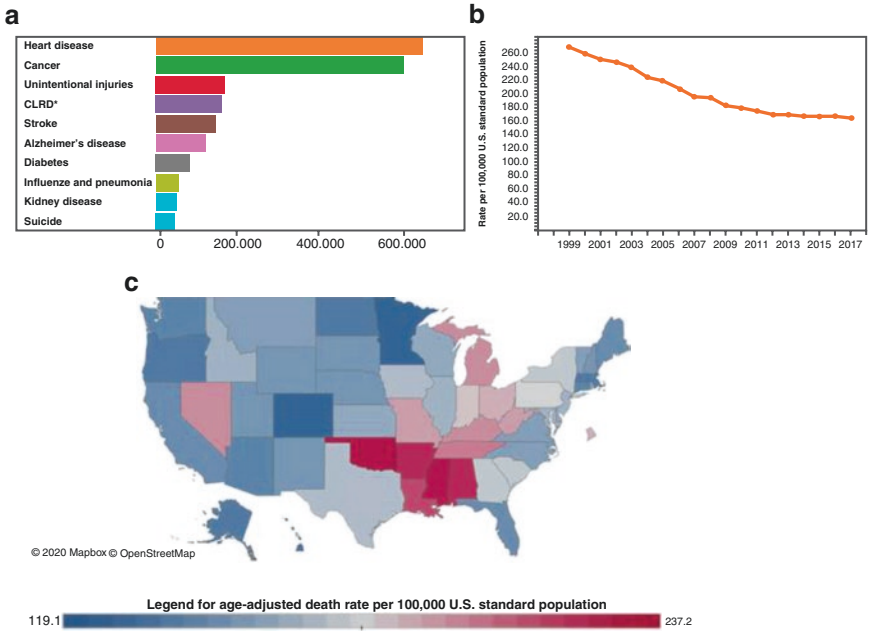

Fig. 1 Number of deaths and age-adjusted mortality rate for heart disease in the USA, overall and by state in 2017 (NCHS Data Visualization Tool). (**a**) Number of deaths for the ten leading causes of the death in the USA. (**b**) Age-adjusted mortality rate due to heart disease in the USA, 1999–2007. (**c**) Age-adjusted mortality rate due to heart disease in the USA by state, 2017

Million Hearts Initiative [19], and the World Health Organization [20] are unlikely to be reached. In the face of this uncertainty, it is now imperative to gain a deeper understanding of past trends in fatal and nonfatal CVD rates and risk factors to inform potential interventions on an individual and population level in the USA and globally.

2 Overall Cardiovascular Disease Mortality and Morbidity

2.1 Cardiovascular Disease Mortality

Total deaths in the USA attributed to major CVD (*International Classification of Diseases, Tenth Revision* [*ICD-10*] codes I00-I78) in 2018 were 863,834 (an 11% increase compared with 2011) [21]. Deceleration in the decline of age-adjusted mortality rate (AAMR) due to CVD was first observed and reported by examining data from 1999 to 2014 by Sidney et al. [9] and was confirmed in a recent time-trend analysis incorporating mortality data through 2017 by Shah et al. [1] using the Joinpoint Regression Program (National Cancer Institute) [22]. Specifically, the rate

of AAMR declines for heart disease was −8.3 (95% confidence interval [CI] −8.8, −7.8) indicating that 8.3 fewer deaths per 100,000 population occurred per year between 1999 and 2010. This substantially slowed subsequently with a rate of decline of −1.8 (−2.5, −1.0) between 2010 and 2017.

Significant heterogeneity in CVD mortality exists across states (Fig. 1c); observed declines between 1999 and 2016 varied widely and were largely attributable to cardiovascular risk factors [23]. Disparities in CVD mortality also exist on a county level, and rural counties in the "US heartland" in southeastern Oklahoma, the Mississippi River Valley, and Eastern Kentucky bore a disproportionate burden of counties at >90th percentile for CVD mortality, whereas the lowest CVD mortality rates were observed in counties in California, Colorado, Nebraska, Minnesota, Virginia, and Florida [24].

Marked disparities persist in CVD mortality in that non-Hispanic blacks (NHB) compared with NH whites have higher AAMR for CVD with the highest CVD AAMR occurring in NHB men (Fig. 2) [3, 25, 26]. Further, these disparities have remained largely unchanged over time and are likely attributable to multiple factors, such as access to healthcare, disease management, and delivery of care as well as general societal and structural contributors to health and disease (e.g., income, education, safe housing, racism) [27]. Limited data on American Indians/Alaska Natives likely obscure the burden of CVD mortality in this population subgroup and lack of mortality data on disaggregated Hispanic and Asian subgroups makes it challenging to interpret mortality differences.

Of note, the burden of CVD mortality is greatest among older adults aged 65 years and older who represented over 80% of all CVD deaths in 2018 [2]. The total US population of older adults has increased significantly with 50.9 million adults aged 65 years and older in 2017 (22.9% total increase between 2011 and 2017). Despite declines in AAMR, the growth of the aging population accounts for a significant increase in total CVD deaths. Given projections of the population of older adults to increase to 73.1 million by 2030 (44% increase estimated between 2017 and 2030), innovative strategies to prevent and manage CVD are needed that target the morbidity and mortality in this growing "baby boomer" subgroup.

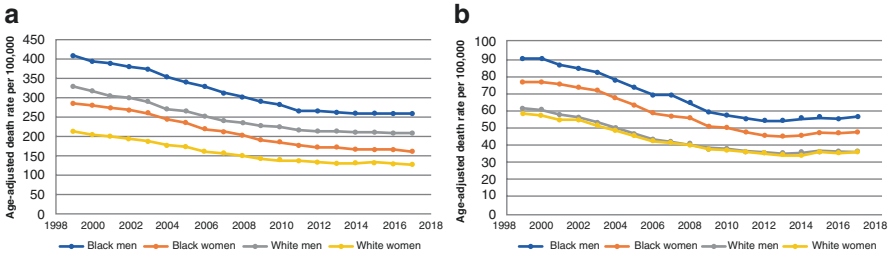

Fig. 2 Trends in cardiovascular mortality by race-sex subgroups due to heart disease and stroke in the USA from vital statistics using the centers for disease control wide-ranging online data for epidemiologic research data source, 1999–2017. (**a**) Heart diseases. (**b**) Cerebrovascular diseases

2.2 Cardiovascular Disease Morbidity

Prevalence of CVD (comprising of CHD, stroke, HF, and hypertension) in adults aged ≥20 years and older is estimated to be 48.0% overall (representing 121.5 million adults in 2016) based on data from the National Health and Nutrition Examination Survey 2013 to 2016 data [3]. Excluding hypertension, CVD prevalence is 9.0% representing 24.3 million adults in 2016. Age-adjusted prevalence of heart disease varied by race/ethnicity (11.0%, 9.7%, 7.4%, and 6.1% among whites, blacks, Hispanics, and Asians, respectively). Healthcare utilization for CVD remains high with increases in the number of hospital discharges from 1993 to 2016 with approximately 4,840,000 inpatient discharges with CVD as a principal diagnosis in 2016 based on the Healthcare Cost and Utilization Project (HCUP) data [3]. In addition, there were 4,774,000 visits to the emergency department (ED) and 72,128,000 physician office visits with a primary diagnosis of CVD in 2016 based on National Ambulatory Medical Care Survey (NAMCS) data [3].

3 Mortality and Morbidity Attributable to CVD Subtypes in the USA

Subtypes of HD, such as CHD, stroke, heart failure (HF), and hypertension, are heterogeneous in their pathophysiology and contribution toward preventable fatal and nonfatal CVD events. Therefore, in order to facilitate targeted efforts to reduce the national burden of CVD, it is important to delineate cause-specific patterns in CVD morbidity and mortality that have significant variability.

3.1 Coronary Heart Disease

Total deaths attributed to CHD (*ICD 10* codes I20-I28) in 2018 were 365,744 (a 3% decrease compared with 2011), which represents the largest subgroup of deaths due to CVD [21]. Rates of decline in CHD followed similar patterns to overall CVD trends with deceleration in decline of ischemic heart disease (IHD) AAMR (mean annual rate of change −2.7% per year between 2011 and 2015 compared with −5.0% per year between 2000 and 2011) [28]. This inflection point in 2011 was statistically significant in the overall population as well as in men and women and among NH whites, NH blacks, and Hispanic adults. As for total CVD, NH blacks had the highest AAMR due to CHD.

An estimated 18.2 million American adults have CHD based on self-reported data from the 2013–2016 NHANES survey cycles with an overall prevalence of 6.7% [3]. Based on data from the 2017 National Health Interview Survey, prevalence of CHD is estimated to be highest among blacks (5.9%) compared with whites

(5.6%), Asians (4.3%), and American Indian/Alaska Natives (2.7%) [3]. While the overall body of literature identifies a decline in the incidence of CHD over time, emerging data from the Atherosclerosis Risk in Communities Study identified an increase in the proportion of hospitalizations for acute myocardial infarction (MI) occurring among younger adults (35–54 years) from 25% to 32% of all hospitalizations for MIs between 1995 and 2014 [29].

There are multiple factors that may contribute to both the decline and now the overall deceleration in the decline in CHD deaths in the USA over the past several decades, including heterogeneous changes in cardiovascular risk factor burden as well as remarkable advances in medical, surgical, and device treatments for CVD. When applying the widely validated IMPACT model to CHD mortality data between 1980 and 2000, reductions in major cardiovascular risk factors (total cholesterol, systolic blood pressures, rates of cigarette smoking) accounted for approximately 61% of the decrease in CHD deaths [5]. However, this was offset, in part, by increases in body mass index and prevalence of diabetes, which resulted in approximately 25,905 and 33,465 additional deaths, respectively. Approximately 47% of deaths prevented were explained by changes in medical treatments, predominantly secondary prevention. This highlights that prior to 2000, even before the deceleration observed in 2011, increases in the rates of obesity and diabetes were beginning to contribute to excess CHD mortality. These data inform future individual-level and population-based prevention strategies targeting prevention of risk factors as well as dissemination and implementation to enhance uptake of evidence-based medical therapies for CHD.

3.2 Stroke and Transient Ischemic Attack

Total deaths attributed to cerebrovascular diseases or stroke (*ICD 10* codes I60-I69) in 2018 were 147,810 (a 15% increase compared with 2011) [21]. When separated from aggregate CVD mortality, stroke ranks fifth among all causes of death, behind heart disease, cancer, respiratory diseases, and unintentional injuries/accidents [3]. AAMR from 1999 to 2017 experienced an inflection point in 2011, similar to overall CVD with the rate of AAMR decline between 1999 and 2011 of −2.3 deaths per 100,000/year with no significant change in AAMR between 2011 and 2017 [1]. Similar disparities were observed in mortality due to stroke with stroke AAMR for NH black adults compared with NH white, NH Asian, NH Indian or Alaska Native, and adults in the USA [3]. There are also significant disparities geographically for stroke mortality with the approximately 30 to 40% higher rates in the southeastern USA, termed the “stroke belt,” that have persisted since 1940 [24].

Based on data from NHANES 2013 to 2016, stroke prevalence was estimated to be 2.5% representing 7.0 million American adults [3]. Projections predict a 21% increase in prevalence of stroke by 2030 [30]. Stroke events annually exceed 790,000, of which 30% are recurrent stroke events, approximately 87% are ischemic, and 13% are hemorrhagic [3]. Prevalence of transient ischemic attacks is

limited based on awareness, but is estimated to be at least 2.3% or five million adults in the USA. Hospitalization rates for acute ischemic stroke have largely remained stable or increased over time in younger adults (25–59 years), but have declined for older adults (≥60 years) [31, 32]. Black-white disparities in stroke are greater among younger adults with incidence rate ratio (IRR) of 4.02 for those aged 45–54 years, whereas overall age- and sex-adjusted IRR was 1.51 [33, 34]. In 2016, 874,000 inpatient discharges, 590,000 ED visits, and 2,155,000 physician office visits with stroke as the principal or first-listed diagnosis occurred [3].

3.3 Heart Failure

Total deaths attributed to HF (*ICD 10* codes I50) in 2018 as an underlying cause of death and multiple cause of death (i.e., any mention on the death certificate) were 83,616 (a 43% increase compared with 2011) and 366,464 (a 29% increase compared with 2011), respectively [21]. Surveillance statistics measuring mortality related to HF are fraught with coding issues in that HF is not considered an underlying cause of death by nosologists, but a mode of death, and the underlying cause of death should be listed as the disease process leading to HF (e.g., CHD) [35]. As a result of coding recommendations for death certificates to discourage the recording of HF as the underlying cause of death, any mention of HF on the death certificate represents a more comprehensive burden of mortality related to HF. However, this still does not allow distinction between the two major subtypes of HF that share similar case fatality rates: HF with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF). Between 2000 and 2011, the AAMR of HF as any mention decreased and reversed with increasing AAMR subsequently [28]. Relative increases in HF AAMR were greatest among younger adults (<65 years), but the absolute burden of HF deaths was greatest among older adults (≥65 years) [2, 36]. Numerous studies have outlined the adverse consequences of a national policy, the Hospital Readmissions Reduction Program established by the Centers for Medicare and Medicaid Services to impose financial penalties on hospitals with higher-than-expected 30-day readmission rates in patients with HF that may also be contributing, in part, to increasing mortality trends [37–39].

Prevalence of HF is estimated to be 6.2 million among American adults based on NHANES 2013 to 2016 with projections estimating the prevalence will increase to >8 million (a 46% increase) by 2030 based on the aging population [3, 40]. Decrease in the incidence of HF was reported in data from Olmsted County between 2000 and 2010 (315.8 vs. 219.3 per 100,000) [41]. Despite these promising data, overall remaining lifetime risk for HF remains high and is estimated to range from 20 to 45% at age 45 years in data from the Cardiovascular Lifetime Risk Pooling project [42]. Burden of hospitalized HF remains high with 809,000 discharges in 2016. In addition, 1,932,000 physician office visits and 414,000 ED visits for HF occurred in 2016 [3]. Heterogeneous trends within HF for HFrEF and HFpEF are even more challenging to account for in the absence of a national surveillance system. Registry,

electronic health record, and cohort data suggest that HFpEF is now the predominant cause of HF and is expected to increase in the context of the aging population and increasing rates of obesity and diabetes [43, 44]. Contemporary data from Get With the Guidelines that was linked to Medicare identify from a total of 39,982 patients from 254 hospitals between 2005 and 2019 that 46% had HFpEF (≥50%), 8.2% had borderline EF (40–49%), and 46% had HFrEF (<40%) with median survival of 2.1 years. All three types of HF had similar 5-year mortality rates [45, 46]. Patients with HFpEF had the greatest risk of all-cause readmission, but HF with borderline EF and HFrEF had higher rates of cardiovascular and HF readmissions.

3.4 Hypertension

Total deaths attributed to hypertension (*ICD 10* codes I10-I15) in 2018 as an underlying cause of death and multiple cause of death (or any mention) were 95,876 (a 123% increase compared with 1999) and 494,873 (a 323% increase compared with 1999), respectively [21]. Significant race disparities in hypertension-related mortality exist with age-adjusted mortality rates for hypertension as an underlying cause of death in 2017 estimated to be twice as high for NH black compared with NH white men and women (54.1 vs. 23.0 and 37.8 vs. 18.6 per 100,000, respectively) [3]. Since hypertension is relatively infrequently the direct cause of death, examining any mention of hypertension on the death certificate provides a broader and more comprehensive burden of mortality related to HTN. Age-adjusted mortality rate for hypertension as any mention was similarly higher in 2017 for NH black compared with NH white men and women (224.9 vs. 132.9 and 155.3 vs. 99.8 per 100,000, respectively). It is also important to note that these mortality estimates are based on ICD coding for hypertension and not threshold values of blood pressure.

Changing definitions of hypertension have led to widely different published prevalence rates in the literature. Hypertension is also further complicated by different subtypes, including white-coat hypertension and masked hypertension that are harder to identify based on ambulatory clinic blood pressure readings alone. Overall prevalence of hypertension in the USA is high and estimated to be 46.0% based on data from NHANES 2013 to 2016 representing 116.4 million adults based on systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 or on antihypertensive medication using the latest 2017 definition [3]. Estimates across the spectrum of BP categories include approximately 42.3%, 12.1%, 13.7%, and 7.7% with BP readings <120/80, 120 to 129/<80, 130 to 139/80 to 89, and ≥140/90 mm Hg for those not on treatment based on data from NHANES 2011–2014 [47]. Treatment-resistant hypertension is also an important form of hypertension that is associated with high rates of CVD morbidity and mortality and is estimated to complicate approximately 13.7% of cases and increases to 40.4% in a high-risk population of chronic kidney disease [48]. In 2016, hospital discharges with hypertension as the principal diagnosis and any listing were 486,000 and 16,676,000, respectively. Eliminating hypertension is likely to have the most significant impact on reducing

CVD mortality compared with elimination of all other risk factors in women and all other risk factors except smoking in men and is estimated to potentially reduce CVD mortality by 30.4% and 38.0% among men and women, respectively [49].

3.5 Other Cardiovascular Disease

Burden of CVD can also be attributed to additional subtypes of heart disease, such as valvular heart disease, congenital heart disease, and arrhythmias.

Total deaths attributed to valvular heart disease (*ICD 10* codes I34-I38) in 2017 as an underlying cause of death and multiple cause of death (or any mention) were 24,811 and 52,939, respectively. In 2016, 120,000 hospital discharges were for valvular heart disease. Overall prevalence of undiagnosed moderate or severe valvular disease in a primary care population in Europe that was screened with echocardiography was 6.4% [50].

Congenital heart disease is a common form of CVD that represents a growing proportion of adults with CVD given improvement in health outcomes and survival into adulthood. In 2017, mortality related to congenital heart disease was estimated to contribute to 2906 deaths or 0.9 per 100,000 population. In 2010, the estimated prevalence of congenital heart disease was 2.4 million and, in 2016, accounted for 45,000 total hospital discharges. The annual birth prevalence ranges from 2.4 to 13.7 per 1000 live births.

Overall arrhythmias with any mention of disorder of heart rhythm contributed to 558,408 deaths in 2017. The most common disordered heart rhythm is atrial fibrillation and atrial flutter. In 2017, atrial fibrillation was listed as an underlying cause of death in 26,077 and any-mention mortality on 166,793 death certificates. Prevalence of atrial fibrillation in the USA was estimated to be 5.2 million in 2010 with projections increasing to 12.1 million by 2030.

4 Prevalence of Ideal Cardiovascular Health Factor Levels

CVD develops across the life span as the cumulative product of early life and chronic exposures from the environment and health behaviors (e.g., adverse diet, low physical activity, smoking) and the development of risk factors (overweight/obesity, elevated blood pressure, dyslipidemia, dysglycemia) leading to clinical CVD events. However, this progression to CVD during the life course is eminently preventable through individual and population *primordial prevention* strategies, focused from birth on lifestyle and environment to maintain higher stock of health and prevent the development of causal risk factors, and *primary prevention* strategies that identify individuals at risk for incident CVD and attempt to intervene with lifestyle or drug therapies (e.g., weight loss, smoking cessation, statins, antihypertensive therapy. In 2010, the AHA developed and defined a new construct of

Table 1 American Heart Association definition of poor, intermediate, and ideal cardiovascular health for each metric

	Level of cardiovascular health for each metric		
	Poor	Intermediate	Ideal
Current smoking	Yes	Former <12 months	Never or quit ≥12 months
Body mass index	≥30 kg/m^2	25–29.9 kg/m^2	<25 kg/m^2
Physical activity	None	1–149 min/week moderate or 1–74 min/week vigorous or combination	≥150 min/week moderate or ≥75 min/week vigorous or combination
Diet pattern[a], no of components	0–1	2–3	4–5
Total cholesterol	≥240	200–239 or treated to goal	<200
Blood pressure	SBP ≥140 or DBP ≥90	SBP 120–139 mm Hg or DBP 80–89 mm Hg or treated to goal	<120 mm Hg/ <80 mm Hg
Fasting plasma glucose, mg/dL	≥126	100–125 or treated to goal	<100

Adapted from Lloyd-Jones et al. [17] with permission from Wolters Kluwer Health, Inc.
[a]In the context of a healthy dietary pattern that is consistent with a Dietary Approaches to Stop Hypertension-type eating pattern, to consume ≥4.5 cups/day of fruits and vegetables, ≥2 servings/wk of fish, and ≥3 servings/day of whole grains and no more than 36 oz/week of sugar-sweetened beverages and 1500 mg/day of sodium

"cardiovascular health" (CVH), to help quantify CVH in individuals and the population, monitor it over time, and potentially modify it to prevent CVD (Table 1).

In 2010, the AHA developed and defined a new construct of "cardiovascular health" (CVH), to help quantify CVH in individuals and the population, monitor it over time, and potentially modify it to prevent CVD [17]. The full spectrum of CVH can be assessed through the presence and levels of health behaviors and factors: smoking status, physical activity, diet, body mass index, cholesterol, blood pressure, and fasting glucose.

Unfortunately, CV health typically declines from childhood through adolescence to young adulthood and into middle age [51–54]. In a recent study describing trajectories of CVH from young adulthood to midlife using pooled data from five prospective cohorts (the Cardiovascular Risk in Young Finns Study (YFS), Bogalusa Heart Study (BHS), Project Heartbeat, the Special Turku Coronary Risk Factor Intervention Project (STRIP), and the Coronary Artery Risk Development in Young Adults (CARDIA) study), levels of intermediate CVH were present in 25% of the cohort as early as 8 years of age with subsequent declines in CVH. Further, long-term trajectories of CVH were shown to be associated with subclinical atherosclerosis in midlife (carotid intima-media thickness) [55]. These data are consistent with numerous other studies linking favorable CVH with reduction of CVD and non-CVD morbidity, compression of morbidity toward the end of life, and lengthening of health span in multiple population-based cohort studies as well as lower risk

of atherosclerotic CVD in an electronic health record cohort [56–62]. However, few US adults maintain this ideal CV health profile into middle age, and cumulative exposure to intermediate or poor CVH over the lifetime is associated with adverse outcomes highlighting the importance of prevention efforts earlier in the life course [63, 64]. In fact, NHANES data from 2013 to 2016 estimate that <1% of adults meet criteria for ideal levels of five or more CVH metrics.

Despite major health promotion efforts by organizations such as the AHA to improve CVH of all Americans by 2020, the 2012 forecast of only a 6% improvement in population CVH by 2020 is on track to be accurate [63]. However, deterioration of CVH is not an inevitable consequence of aging; it is highly preventable. Behavioral and environmental factors, including policies, play a powerful role in preservation or loss of optimal health factor levels with aging, while genetic factors account for <20% of the variance in maintenance of ideal CV health into middle age [65, 66]. A recent study demonstrated that 60% of young adults who follow five healthy lifestyles (body mass index <25 kg/m^2, no or moderate alcohol intake, healthy diet pattern, healthy physical activity levels, and no smoking) achieve ideal CV health into middle age compared with just 3% of those with no healthy lifestyles [67]. Finally, race disparities in CVH metrics persist [64].

It remains critically important to identify and provide the evidence basis for optimal population-wide strategies that will preserve ideal CVH status from younger life into middle age and beyond and restore greater CVH when possible in middle and older ages. One potential target for CVH promotion that can enhance prevention efforts is 50 × 50 × 50 representing a bold goal to achieve a prevalence of ideal CVH ≥50% in all segments of the population less than age 50 years by 2050 in order to equitably achieve the CVD endgame for all [68].

5 Global Burden of Cardiovascular Disease

Approximately 18 million deaths worldwide annually are due to CVD, a number estimated to increase to 23.6 million by 2030 [69, 70]. Data from the World Economic Forum highlights that CVD now represents 50% of noncommunicable disease and preventable deaths and represents 37% of noncommunicable disease deaths in individuals <70 years [71]. Within Europe, estimates from the European Society of Cardiology in 2017 highlighted that AAMR per 100,000 population were higher in men compared with women in both high-income (410 vs. 283) and middle-income (1019 vs. 790) countries, and in general, AAMR for both men and women are higher in middle-income compared with high-income countries [72]. While AAMR have declined since 1990, there is suggestion of a plateau similar to the US CVD mortality trends. In terms of years of life lost due to CVD, estimates are 38 million and 28 million for men and women, respectively, which accounts for a greater proportion of life lost within middle-income compared with high-income countries. However, patterns of CVD, including CHD, stroke, rheumatic heart disease, and other heart disease, are heterogeneous, globally. For example, in China,

prevalence of CHD is lower, but stroke prevalence is much higher compared with Western countries [73].

Overall, a large proportion of the global CVD burden is estimated to be borne by low- and middle-income countries (~70% of CVD deaths, Fig. 3) [74]. The Global Burden of Disease (GBD) 2017 Study, which utilizes statistical models and available national data on nonfatal and fatal CVD events for 359 diseases and injuries in 195 countries and territories, estimated that the highest mortality rates attributable to CVD were in Central Asia and Eastern Europe. In a recent sub-study from GBD focusing on countries that constitute approximately 50% of the global population and are undergoing rapid economic development (Brazil, Russia, India, China, and South Africa), a time trend analysis between 1992 and 2016 described that the AAMR decline was only −17%, approximately half of that reported in North America during this same period (−39%) [75]. Within countries, Brazil had the largest decline in AAMR, India had very little decline, and South Africa was the only country where the AAMR for CVD actually increased. In addition to reporting AAMR statistics, the GBD program has also estimated that within the USA and worldwide, a large proportion of preventable CVD deaths are due to poor dietary quality, hypertension, obesity, hyperlipidemia, diabetes, smoking, and physical inactivity [76].

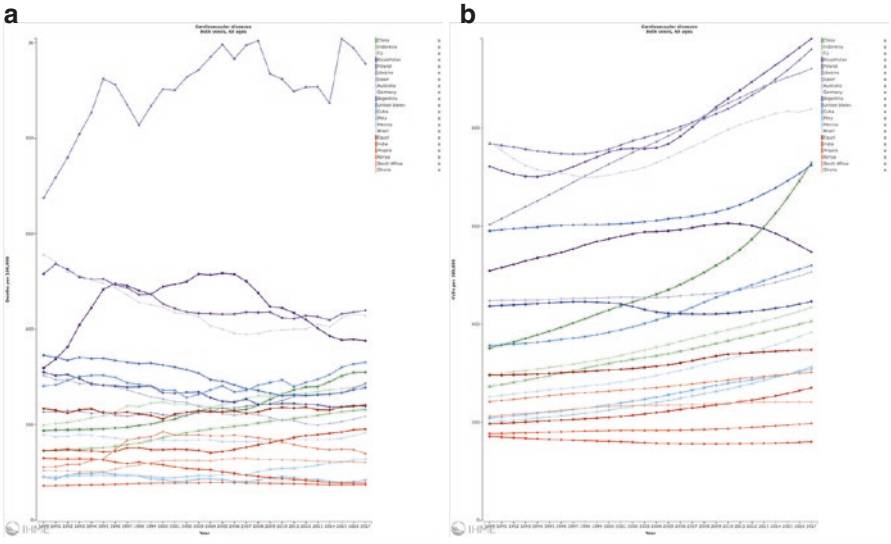

Fig. 3 Global deaths due to cardiovascular disease and years of life lost in all ages and both sexes by country from the Institute for Health Metrics and Evaluation/Global Burden of Disease Collaboration. (**a**) Total cardiovascular disease deaths per 100,000. (**b**) Years of life lost per 100,000

6 Conclusion

In summary, concerning trends in HF and hypertension-related mortality have offset gains achieved in CHD mortality over the past several decades. Increasing prevalence of CVD morbidity is likely in part related to higher rates of obesity, diabetes, and the growth of the aging population. Promotion of CVH across the life course is necessary to focus on primordial and primary prevention strategies and optimization and maintenance of CVH into older adulthood to achieve relative and absolute compression of morbidity. Efforts such as the Million Hearts Initiative can be strengthened by bold and disruptive goals that offer an explicit target and timeline such as 50x50x50 (e.g., achieve a prevalence of ≥50% of all segments of the population less than age 50 years by 2050) to equitably achieve the CVD endgame for all [68, 77]. Multilevel interventions are needed focused on dissemination and implementation of evidence-based therapies at the individual level as well as policy changes at the population level (e.g., smoking bans) to reverse these concerning trends in CVD disease morbidity and mortality in the USA and worldwide.

References

1. Shah NS, Lloyd-Jones DM, O'Flaherty M, et al. Trends in cardiometabolic mortality in the United States, 1999-2017. JAMA. 2019;322(8):780–2.
2. Sidney S, Go AS, Jaffe MG, Solomon MD, Ambrosy AP, Rana JS. Association between aging of the US population and heart disease mortality from 2011 to 2017. JAMA Cardiol. 2019;4(12):1280.
3. Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. Circulation. 2020;141(9):e139–596.
4. National Heart, Lung, and Blood Institute. U.S. Department of Health and Human Services National Institutes of Health. Fact book. 2012.
5. Ford ES, Ajani UA, Croft JB, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. N Engl J Med. 2007;356(23):2388–98.
6. National Vital Statistics System, mortality data (see http://www.cdc.gov/nchs/deaths.htm); and CDC WONDER (see http://wonder.cdc.gov).
7. Ritchey MD, Loustalot F, Bowman BA, Hong Y. Trends in mortality rates by subtypes of heart disease in the United States, 2000-2010. JAMA. 2014;312(19):2037–9.
8. Ma J, Ward EM, Siegel RL, Jemal A. Temporal trends in mortality in the United States, 1969-2013. JAMA. 2015;314(16):1731–9.
9. Sidney S, Quesenberry CP Jr, Jaffe MG, et al. Recent trends in cardiovascular mortality in the United States and public health goals. JAMA Cardiol. 2016;1(5):594–9.
10. Curtin SC. Trends in cancer and heart disease death rates among adults aged 45-64: United States, 1999-2017. Natl Vital Stat Rep. 2019;68(5):1–9.
11. Woolf SH, Schoomaker H. Life expectancy and mortality rates in the United States, 1959-2017. JAMA. 2019;322(20):1996–2016.
12. Mehta NK, Abrams LR, Myrskyla M. US life expectancy stalls due to cardiovascular disease, not drug deaths. Proc Natl Acad Sci U S A. 2020;117(13):6998–7000.
13. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. Circulation. 2018;137(12):e67–e492.

14. Heidenreich PA, Trogdon JG, Khavjou OA, et al. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. Circulation. 2011;123(8):933–44.
15. Khavjou OA. Projections of cardiovascular disease prevalence and costs 2015–2035. 2016. http://www.heart.org/idc/groups/ahaeccpublic/@wcm/@global/documents/downloadable/ucm_491130.pdf
16. Lloyd-Jones DM. Slowing progress in cardiovascular mortality rates: you reap what you sow. JAMA Cardiol. 2016;1(5):599–600.
17. Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic impact goal through 2020 and beyond. Circulation. 2010;121(4):586–613.
18. Angell SY, McConnell MV, Anderson CAM, et al. The American Heart Association 2030 impact goal: a presidential advisory from the American Heart Association. Circulation. 2020;141(9):e120–38.
19. Frieden TR, Berwick DM. The "Million Hearts" initiative--preventing heart attacks and strokes. N Engl J Med. 2011;365(13):e27.
20. Sacco RL, Roth GA, Reddy KS, et al. The heart of 25 by 25: achieving the goal of reducing global and regional premature deaths from cardiovascular diseases and stroke: a modeling study from the American Heart Association and World Heart Federation. Circulation. 2016;133(23):e674–90.
21. National Center for Health Statistics. Multiple cause of death 1999–2018 on CDC WONDER online database, released in 2020. Data are from the Multiple Cause of Death Files, 1999–2018, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at http://wonder.cdc.gov/mcd-icd10.html on Mar 24, 2020 6:01:43 AM.
22. Institute NC. Joinpoint regression program, version 4.7.0.0 - February 2019; Statistical methodology and applications branch, surveillance research program. In Software Citation: Joinpoint Regression Program, Version 4.8.0.1 - April 2020; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute. https://surveillance.cancer.gov/help/joinpoint/tech-help/citation.
23. Global Burden of Cardiovascular Diseases Collaboration, Roth GA, Johnson CO, et al. The burden of cardiovascular diseases among US states, 1990-2016. JAMA Cardiol. 2018;3(5):375–89.
24. Roth GA, Dwyer-Lindgren L, Bertozzi-Villa A, et al. Trends and patterns of geographic variation in cardiovascular mortality among US counties, 1980-2014. JAMA. 2017;317(19):1976–92.
25. Mensah GA, Mokdad AH, Ford ES, Greenlund KJ, Croft JB. State of disparities in cardiovascular health in the United States. Circulation. 2005;111(10):1233–41.
26. Mensah GA, Roth GA, Sampson UK, et al. Mortality from cardiovascular diseases in sub-Saharan Africa, 1990-2013: a systematic analysis of data from the Global Burden of Disease Study 2013. Cardiovasc J Afr. 2015;26(2 Suppl 1):S6–10.
27. Mensah GA, Cooper RS, Siega-Riz AM, et al. Reducing cardiovascular disparities through community-engaged implementation research: a National Heart, Lung, and Blood Institute workshop report. Circ Res. 2018;122(2):213–30.
28. Sidney S, Quesenberry CP Jr, Jaffe MG, Sorel M, Go AS, Rana JS. Heterogeneity in national U.S. mortality trends within heart disease subgroups, 2000-2015. BMC Cardiovasc Disord. 2017;17(1):192.
29. Arora S, Stouffer GA, Kucharska-Newton AM, et al. Twenty year trends and sex differences in young adults hospitalized with acute myocardial infarction. Circulation. 2019;139(8):1047–56.
30. Ovbiagele B, Goldstein LB, Higashida RT, et al. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. Stroke. 2013;44(8):2361–75.
31. George MG, Tong X, Bowman BA. Prevalence of cardiovascular risk factors and strokes in younger adults. JAMA Neurol. 2017;74(6):695–703.

32. Koton S, Schneider AL, Rosamond WD, et al. Stroke incidence and mortality trends in US communities, 1987 to 2011. JAMA. 2014;312(3):259–68.
33. Howard VJ, Kleindorfer DO, Judd SE, et al. Disparities in stroke incidence contributing to disparities in stroke mortality. Ann Neurol. 2011;69(4):619–27.
34. Kleindorfer D, Broderick J, Khoury J, et al. The unchanging incidence and case-fatality of stroke in the 1990s: a population-based study. Stroke. 2006;37(10):2473–8.
35. Foreman KJ, Naghavi M, Ezzati M. Improving the usefulness of US mortality data: new methods for reclassification of underlying cause of death. Popul Health Metrics. 2016;14:14.
36. Glynn P, Lloyd-Jones DM, Feinstein MJ, Carnethon M, Khan SS. Disparities in cardiovascular mortality related to heart failure in the United States. J Am Coll Cardiol. 2019;73(18):2354–5.
37. McCarthy CP, Vaduganathan M, Patel KV, et al. Association of the New Peer Group-Stratified Method with the reclassification of penalty status in the hospital readmission reduction program. JAMA Netw Open. 2019;2(4):e192987.
38. Wadhera RK, Joynt Maddox KE, Wasfy JH, Haneuse S, Shen C, Yeh RW. Association of the Hospital Readmissions Reduction Program with mortality among medicare beneficiaries hospitalized for heart failure, acute myocardial infarction, and pneumonia. JAMA. 2018;320(24):2542–52.
39. Wadhera RK, Vaduganathan M, Jiang GY, et al. Performance in federal value-based programs of hospitals recognized by the American Heart Association and American College of Cardiology for high-quality heart failure and acute myocardial infarction care. JAMA Cardiol. 2020;5(5):1–8. https://doi.org/10.1001/jamacardio.2020.0001. Online ahead of print. PMID:32074242
40. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. 2013;6(3):606–19.
41. Gerber Y, Weston SA, Redfield MM, et al. A contemporary appraisal of the heart failure epidemic in Olmsted County, Minnesota, 2000 to 2010. JAMA Intern Med. 2015;175(6):996–1004.
42. Huffman MD, Berry JD, Ning H, et al. Lifetime risk for heart failure among white and black Americans: cardiovascular lifetime risk pooling project. J Am Coll Cardiol. 2013;61(14):1510–7.
43. Oktay AA, Rich JD, Shah SJ. The emerging epidemic of heart failure with preserved ejection fraction. Curr Heart Fail Rep. 2013;10(4):401–10.
44. Pandey A, Golwala H, Sheng S, et al. Factors associated with and prognostic implications of cardiac troponin elevation in decompensated heart failure with preserved ejection fraction: findings from the American Heart Association get with the guidelines-heart failure program. JAMA Cardiol. 2017;2(2):136–45.
45. Cheng RK, Cox M, Neely ML, et al. Outcomes in patients with heart failure with preserved, borderline, and reduced ejection fraction in the Medicare population. Am Heart J. 2014;168(5):721–30.
46. Shah KS, Xu H, Matsouaka RA, et al. Heart failure with preserved, borderline, and reduced ejection fraction: 5-year outcomes. J Am Coll Cardiol. 2017;70(20):2476–86.
47. Muntner P, Carey RM, Gidding S, et al. Potential US population impact of the 2017 ACC/AHA high blood pressure guideline. Circulation. 2018;137(2):109–18.
48. Patel KV, Li X, Kondamudi N, et al. Prevalence of apparent treatment-resistant hypertension in the United States according to the 2017 high blood pressure guideline. Mayo Clin Proc. 2019;94(5):776–82.
49. Patel SA, Winkel M, Ali MK, Narayan KM, Mehta NK. Cardiovascular mortality associated with 5 leading risk factors: national and state preventable fractions estimated from survey data. Ann Intern Med. 2015;163(4):245–53.
50. d'Arcy JL, Coffey S, Loudon MA, et al. Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort Study. Eur Heart J. 2016;37(47):3515–22.

51. Gooding HC, Shay CM, Ning H, et al. Optimal lifestyle components in young adulthood are associated with maintaining the ideal cardiovascular health profile into middle age. J Am Heart Assoc. 2015;4(11)
52. Ning H, Labarthe DR, Shay CM, et al. Status of cardiovascular health in US children up to 11 years of age: the National Health and Nutrition Examination Surveys 2003-2010. Circ Cardiovasc Qual Outcomes. 2015;8(2):164–71.
53. Shay CM, Ning H, Allen NB, et al. Status of cardiovascular health in US adults: prevalence estimates from the National Health and Nutrition Examination Surveys (NHANES) 2003-2008. Circulation. 2012;125(1):45–56.
54. Shay CM, Ning H, Daniels SR, Rooks CR, Gidding SS, Lloyd-Jones DM. Status of cardiovascular health in US adolescents: prevalence estimates from the National Health and Nutrition Examination Surveys (NHANES) 2005-2010. Circulation. 2013;127(13):1369–76.
55. Allen NB, Krefman AE, Labarthe D, et al. Cardiovascular health trajectories from childhood through middle age and their association with subclinical atherosclerosis. JAMA Cardiol. 2020;5(5):1–10. https://doi.org/10.1001/jamacardio.2020.0140. Online ahead of print. PMID:32159727
56. Khan SS, Ning H, Wilkins JT, et al. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. JAMA Cardiol. 2018;3(4):280–7.
57. Folsom AR, Yatsuya H, Nettleton JA, et al. Community prevalence of ideal cardiovascular health, by the American Heart Association definition, and relationship with cardiovascular disease incidence. J Am Coll Cardiol. 2011;57(16):1690–6.
58. Allen NB, Zhao L, Liu L, et al. Favorable cardiovascular health, compression of morbidity, and healthcare costs: forty-year follow-up of the CHA study (Chicago Heart Association Detection Project in Industry). Circulation. 2017;135(18):1693–701.
59. Sengelov M, Cheng S, Biering-Sorensen T, et al. Ideal cardiovascular health and the prevalence and severity of aortic stenosis in elderly patients. J Am Heart Assoc. 2018;7(3)
60. Shah AM, Claggett B, Folsom AR, et al. Ideal cardiovascular health during adult life and cardiovascular structure and function among the elderly. Circulation. 2015;132(21):1979–89.
61. Rasmussen-Torvik LJ, Shay CM, Abramson JG, et al. Ideal cardiovascular health is inversely associated with incident cancer: the Atherosclerosis Risk in Communities study. Circulation. 2013;127(12):1270–5.
62. Rana JS, Liu JY, Moffet HH, et al. Risk of atherosclerotic cardiovascular disease by cardiovascular health metric categories in approximately 1 million patients. Eur J Prev Cardiol. 2020:2047487320905025.
63. Huffman MD, Capewell S, Ning H, Shay CM, Ford ES, Lloyd-Jones DM. Cardiovascular health behavior and health factor changes (1988-2008) and projections to 2020: results from the National Health and Nutrition Examination Surveys. Circulation. 2012;125(21):2595–602.
64. Pool LR, Ning H, Lloyd-Jones DM, Allen NB. Trends in racial/ethnic disparities in cardiovascular health among US adults from 1999-2012. J Am Heart Assoc. 2017;6:9.
65. Allen NB, Lloyd-Jones D, Hwang SJ, et al. Genetic loci associated with ideal cardiovascular health: a meta-analysis of genome-wide association studies. Am Heart J. 2016;175:112–20.
66. Allen NB, Hwang S-J, Cupples LA, et al. Abstract 17245: the heritability of ideal cardiovascular health: the Framingham Heart Study. Circulation. 2010;122(Suppl 21):A17245.
67. Liu K, Daviglus ML, Loria CM, et al. Healthy lifestyle through young adulthood and the presence of low cardiovascular disease risk profile in middle age: the Coronary Artery Risk Development in (Young) Adults (CARDIA) study. Circulation. 2012;125(8):996–1004.
68. Labarthe D, Lloyd-Jones DM. 50x50x50: cardiovascular health and the cardiovascular disease endgame. Circulation. 2018;138(10):968–70.
69. Global burden of disease study 2017 (GBD 2017). Seattle: Institute for Health Metrics and Evaluation (IHME), University of Washington; 2018. http://ghdx.healthdata.org/gbd-results-tool. Accessed 1 Apr 2019.
70. Global status report on noncommunicable diseases 2014. Geneva, Switzerland: World Health Organization; 2014. http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854_eng.pdf. Accessed 19 Aug 2019.

71. Bloom DECE, Jané-Llopis E, Abrahams-Gessel S, Bloom LR, Fathima S, Feigl AB, Gaziano T, Mowafi M, Pandya A, et al. The global economic burden of non-communicable diseases. Geneva: World Economic Forum; 2011.
72. Timmis A, Townsend N, Gale CP, et al. European Society of Cardiology: cardiovascular disease statistics 2019. Eur Heart J. 2020;41(1):12–85.
73. Celermajer DS, Chow CK, Marijon E, Anstey NM, Woo KS. Cardiovascular disease in the developing world: prevalences, patterns, and the potential of early disease detection. J Am Coll Cardiol. 2012;60(14):1207–16.
74. Roth GA, Huffman MD, Moran AE, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. Circulation. 2015;132(17):1667–78.
75. Zou Z, Cini K, Dong B, et al. Time trends in cardiovascular disease mortality across the BRICS: an age-period-cohort analysis of key nations with emerging economies using the global burden of disease study 2017. Circulation. 2020;141(10):790–9.
76. US Burden of Disease Collaborators, Mokdad AH, Ballestros K, et al. The state of US health, 1990-2016: burden of diseases, injuries, and risk factors among US states. JAMA. 2018;319(14):1444–72.
77. Ritchey MD, Loustalot F, Wall HK, et al. Million hearts: description of the national surveillance and modeling methodology used to monitor the number of cardiovascular events prevented during 2012-2016. J Am Heart Assoc. 2017;6:5.

Cardiovascular Risk Assessment: From Global Risk Scoring to Risk Enhancing Factors

Rina Mauricio and Amit Khera

Summary

- Primary prevention should begin with assessing ~~for~~ healthy lifestyle habits and determining the patient's absolute risk for developing ASCVD.
- Risk assessment entails determining absolute, global, short-term (i.e., 10 years) risk using validated risk assessment equations. Guidelines support the use of the Pooled Cohort Equations for estimating 10-year global ASCVD risk.
- The currently available risk assessment tools may overestimate or underestimate risk in certain populations. Being cognizant of the strengths and weaknesses of these tools is important when determining an individual patient's risk.
- Risk enhancing factors and, when needed, coronary calcium scores should be taken into consideration for patients at borderline or intermediate risk.
- Guidelines support routine risk assessment in asymptomatic individuals 40 to 75 years old. In individuals 20–39 years old, or those over the age of 75, there is limited evidence for routine risk assessment.
- Risk factors such as diet, physical activity, and obesity, while not included in current risk assessment tools, should still be taken into account when assessing a patient's overall global cardiovascular risk.
- Preventive interventions, such as statin therapy or blood pressure management, should be targeted at high-risk individuals to maximize the benefits of these interventions and minimize harm or overtreatment.

R. Mauricio
Department of Internal Medicine, Division of Cardiology, University of Texas Southwestern, Dallas, TX, USA

A. Khera (✉)
Division of Cardiology, UT Southwestern Medical Center, Dallas, TX, USA
e-mail: amit.khera@utsouthwestern.edu

N. D. Wong et al. (eds.), *ASPC Manual of Preventive Cardiology*,
Contemporary Cardiology, https://doi.org/10.1007/978-3-030-56279-3_3

1 Introduction

Cardiovascular disease (CVD) remains the number 1 cause of death in the United States [1]. Rates of death attributable to CVD had been on the decline. However, despite advances in prevention and treatment, there has been a noticeable increase in CVD mortality in men and women in recent years [1]. Redoubling efforts to reverse this trend requires continued identification of individuals at increased risk for developing CVD. This practice, termed CVD risk assessment, remains a cornerstone of prevention efforts.

Our understanding of risk assessment has greatly evolved from focusing on individual risk factors to determining global cardiovascular risk. Risk assessment aims to find those individuals who are at the highest absolute risk and target primary prevention therapies at this cohort [2]. Risk assessment currently focuses on short-term risk (i.e., 10-year risk). Assessing long-term or lifetime risk may be beneficial for certain individuals. This chapter focuses on methods to determine short-term cardiovascular risk, the rationale for doing so, and potential pitfalls to current risk assessment tools.

2 The High-Risk Approach and Shifting Toward Risk Assessment Equations

When assessing an individual's short-term risk for cardiovascular disease, the focus should be on absolute risk, rather than relative risk [3, 4]. Relative risk is an exposed individual's risk for a given outcome relative to nonexposed individuals. For example, an individual smoker will have a higher relative risk for developing lung cancer compared to a nonsmoker. The shortcomings of this type of risk assessment are that it is always in reference to the baseline population and is dependent on heterogeneity of the exposure. If a population was comprised entirely of smokers, relative risk would be the same between each individual, despite the fact that absolute risk for disease is high. Further, Fig. 1 shows the effect of treatment on low, absolute risk individuals (without a history of vascular disease, i.e., primary prevention) versus high, absolute risk individuals (prior history of vascular disease, i.e., secondary prevention). After treatment, both groups had a 24% relative risk reduction but marked differences in absolute risk reduction: 2.0% in the low, absolute risk group vs. 3.4% in the high, absolute risk group. Thus, the greatest clinical benefit is in those at high, absolute risk. Preventive interventions, such as statin therapy or blood pressure management, should be targeted at individuals at high, absolute risk to maximize the benefits of these interventions and minimize harm or overtreatment.

There are two different but complementary strategies for CVD preventions, termed the high-risk and population-based approaches [2]. The population-based strategy aims to lower the mean level of risk factors in the population with the goal of favorably shifting the overall prevalence of the disease, largely through public

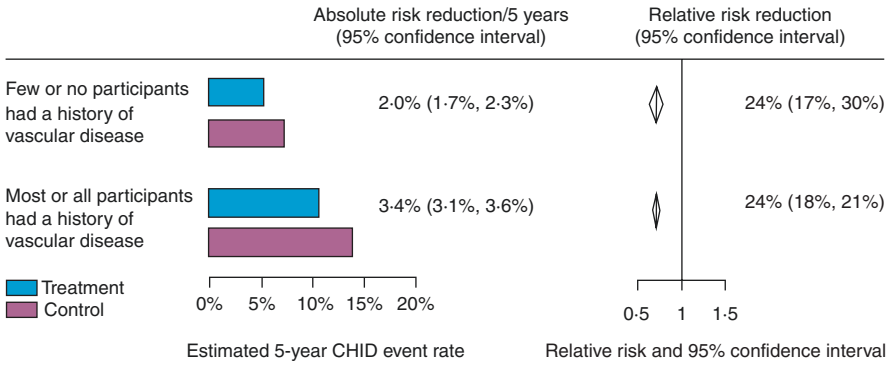

Fig. 1 Absolute and relative treatment effects on coronary heart disease in cholesterol-lowering trials by history of vascular disease. (Reprinted from Jackson et al. [101]. With permission from Elsevier)

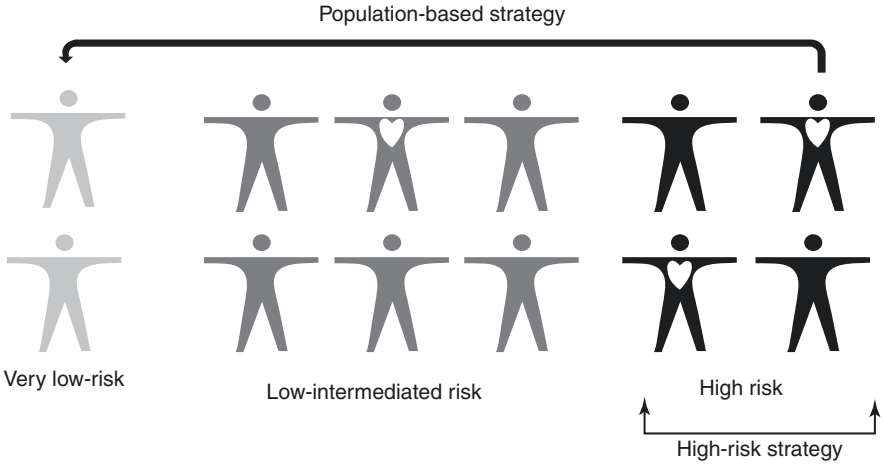

Fig. 2 Population-based strategy versus high-risk strategy. (Reprinted from Khera [102]. With permission from Springer Nature)

health measures. This is a powerful strategy with potential for large effects on population health, but it can also lead to overtreatment of a sizeable number of individuals. For example, population-wide efforts to discourage vaping may meaningfully reduce the number of individuals who vape, but these initiatives will also target individuals who do not vape, offering them little direct benefit.

In the population as a whole, only a select group of individuals are high risk for developing CVD and merit high intensity intervention. This high-risk or "medical" approach is more commonly encountered in office-based practice and involves setting a threshold of risk and focusing treatment strategies on individuals who exceed this risk (Fig. 2). Here, interventions are more targeted to the individual, maximizing

the risk-benefit ratio of any intervention and optimizing cost-effectiveness. A shortcoming is that lower-risk patients who cumulatively have large numbers of cardiovascular events are not treated. A goal of primary prevention, therefore, is to identify those at high, absolute risk and target preventive therapies to these individuals, with the intensity of treatment matching the individual's absolute risk of disease.

2.1 Shifting from Risk Factors to Multivariable Risk Assessment Models

The term cardiovascular "risk factors" originated from the Framingham Heart Study and involves factors whose presence is associated with an increased likelihood that disease will develop at a later time [5, 6]. Since the publication of the seminal paper from the Framingham Heart Study [6], our understanding of cardiac risk factors and cardiovascular risk has grown considerably. Previous assessment of CVD risk relied on assessing and treating each risk factor individually, with lack of a formal integrated method to assess risk [7]. However, individual risk factors poorly discriminate CVD risk, as evidenced by the fact that half of all patients with myocardial infarction have average cholesterol levels for the population. Over time, multivariable risk prediction models were developed, integrating multiple CVD risk factors and demographic data, to more accurately pinpoint an individual's CVD risk into a single score.

The Framingham Heart Study developed one of the first such multivariable risk calculators, which included a model to assess 10-year risk of coronary heart disease (CHD) [8]. The Framingham 10-Year Risk Score for global CHD risk was recommended by the Third Report of the National Cholesterol Education Program Expert Work Group on Diagnosis, Evaluation, and Treatment of High Blood Cholesterol In Adults (ATP III) for the assessment of risk of hard CHD events (myocardial infarction or coronary death) in individuals free of CHD [4]. Over time, Framingham risk assessment models expanded to predict absolute global CVD risk, defined as CHD plus stroke, peripheral arterial disease, and heart failure [9]. The 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk recommended against using the Framingham Risk Score for CHD due to concerns regarding its limited scope and generalizability [10]. The Working Group then developed the Pooled Cohort Equations (PCE), which are now widely incorporated in clinical practice for assessment of global CV risk and to guide initiation of preventive therapy.

3 Using the Pooled Cohort Equations to Assess Cardiovascular Risk

The Working Group of the 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk identified two reasons for developing the PCE. First, the Framingham Risk Score was derived in an exclusively white population, limiting its

generalizability, and second, it focused only on CHD events, missing an opportunity for stroke prevention. Moreover, the initial Framingham baseline exams began in 1968, now half a century old, at a time when risk factor prevalence and prevention strategies were markedly different from contemporary patient populations. Therefore, the goal was to develop a new risk score that expanded to hard ASCVD events (defined as first occurrence of nonfatal myocardial infarction, CHD death, or fatal or nonfatal stroke) and in more contemporary, multiethnic populations.

The PCE were derived from several large, racially diverse cohort studies, including the Atherosclerosis Risk in Communities (ARIC) study, the Cardiovascular Health Study (CHS), the Coronary Artery Risk Development in Young Adults (CARDIA) study, and the Framingham Original and Offspring Cohort [10]. ARIC, CHS, CARDIA, and the Framingham Offspring Cohort started recruitment in the 1970s–1990s, reflecting more modern cohorts compared to the original Framingham Study, though still lagging in time relative to modern practice. The majority of participants were middle-aged (mean age of 54.7 years old), and all participants were white or African-American. The Working Group specifically chose cohorts with more than 10 years of follow-up.

Similar to the Framingham Risk Score, the PCE incorporates recognized traditional risk factors for CVD: age, sex, race, total cholesterol, high-density lipoprotein cholesterol (HDL-C), systolic blood pressure, antihypertensive treatment, diabetes mellitus, and smoking. At the time of the development of the PCE, several risk scores had been developed including novel risk factors such as high-sensitivity C-reactive protein (hs-CRP) [11, 12], family history, and body mass index (BMI) [13]. Diastolic blood pressure, family history, moderate or severe chronic kidney disease (defined as estimated glomerular filtration rate [GFR] of <60 mL/min/1.73m^2), and BMI were all considered as additional risk factors for inclusion in the final PCE equation, but they did not improve model discrimination. Other potential risk factors, specifically hs-CRP, apolipoprotein B (ApoB), coronary artery calcium (CAC) score, carotid artery intima-media thickness (CIMT), and ankle-brachial index (ABI), could not be evaluated for inclusion in the model as they were not systematically assessed in the included studies.

The result was two risk calculators, one for white and another for African-American individuals, which provide sex- and race-specific estimates of 10-year ASCVD risk for individuals aged 40–79 years. The PCE are recommended for use in non-Hispanic blacks and non-Hispanic whites, reflective of the populations from which it was derived. It also provides estimation of lifetime ASCVD risk for those aged 20–59 years of age.

The Working Group externally validated the PCE in a combined cohort from the Multi-Ethnic Study of Atherosclerosis (MESA) and the REasons for Geographic And Racial Differences in Stroke (REGARDS) studies, as well as contemporary data from the derivation cohorts (ARIC visit 4, Framingham Original Cohort cycle 22 and 23, and Framingham Offspring Cohort cycle 5 or 6). The validation cohort included 13,652 white and African-American individuals 40–79 years old. Although the PCE overpredicted events in the validation group, this was more pronounced in higher-risk rather than lower-risk individuals. Practically, higher-risk individuals would

have met the threshold for treatment, so overestimation of risk in this group would not lead to unnecessary treatment. Since the publication of the PCE, several studies have expanded on shortcomings and additional considerations in their application.

4 Limitations of the Pooled Cohort Equation

Even the earliest tool for global risk assessment, the Framingham Risk Score, noted that their model was limited in individuals with very low CHD incidence rates, such as younger individuals, and in populations that varied from the source population, including those from other countries or ethnic groups. The PCE limited the derivation populations exclusively to white and African-American individuals from cohorts with a 10-year rate of ASCVD ranging from 1.0 to 28.5%, with a median rate of 9.5% [10]. Therefore, its ability to predict risk in other races/ethnicities with event rates dissimilar to these is limited. Although there is no separate equation for Asian-Americans, application of PCE for whites is recommended. However, the PCE can underestimate risk in South Asians and overestimate risk in East Asians [14]. Hispanic and Latino-Americans are a heterogeneous group in terms of ancestry, country of origin, and ASCVD risk. The PCE for whites is the default risk calculator, although the PCE for African-Americans can be used if there is also African ancestry. Additionally, without a large number of older persons in the derivation cohorts, the PCE does not predict risk beyond age 75. Finally, the PCE only estimates hard ASCVD and does not include the risk of softer events or procedures such as unstable angina, bypass surgery, or percutaneous interventions.

4.1 Populations with Lower or Higher CVD Incidence Rates

Subsequent assessments of the PCE outside of the Working Group using modern cohorts demonstrated moderate to good discrimination in some studies [15, 16] and overestimated short-term risk in others [17–20]. Using data from MESA, the PCE overestimated risk by 86% in men and 67% in women [20]. Increased use of preventive therapies in modern cohorts, such as aspirin, lipid-lowering medications, and antihypertensive therapies, did not appear to explain the overestimation of risk [20].

Outside of the United States, in a large, modern, multiethnic cohort, the PCE overestimated risk of ASCVD [21]. Furthermore, degrees of risk were different when comparing individuals of European vs. Chinese or other Asian vs. Indian, Maori, or Pacific Islander ancestry [21]. The PCE also overestimate or underestimate risk in other racial and ethnic groups [22–24]. Indeed, alternative risk prediction models have been developed for non-US populations and are better calibrated for the population from which they were derived [21, 22]. Socioeconomic status also appears to affect the performance of the PCE. The PCE overestimates risk in individuals of higher socioeconomic status [25] and underestimates risk in patients from lower socioeconomic classes [26]. Risk scores that incorporate social

determinants of health more accurately identify high-risk individuals and predict future events [27].

4.2 Young Populations and When to Assess Long-Term or Lifetime Risk

Assessing for the presence of traditional cardiovascular risk factors should begin in young adults starting at age 20–39 years old [28]. However, incorporating these individual risk factors into a global 10-year risk estimate for younger individuals is challenging. First, 20- to 39-year-old individuals were excluded from the PCE derivation cohort. Additionally, using short-term risk calculators such as the PCE or the Framingham Risk Score in younger individuals is limited by the calculators' reliance on age as the dominant risk determinant resulting in low estimated event rates. Determining 30-year (long-term) or lifetime risk may be more applicable in younger individuals.

Studies have shown that optimal risk factor control at middle age confers lower lifetime risk of CVD compared to individuals with two or more major cardiac risk factors in middle age [29–31]. In another study (average age, 40–50 years), low 10-year risk but high lifetime risk has been associated with greater carotid intima media thickness, higher CAC scores, and greater progression of coronary artery calcium [32].

There are few models for estimating 30-year risk of CVD. A model for assessing 30-year risk of hard CVD (coronary death, MI, fatal and nonfatal stroke) events was developed in the Framingham Offspring Cohort [33] and adjusted for the competing risk of non-cardiovascular death. However, this tool is limited given its derivation in an exclusively white cohort that was recruited at a time when risk factor prevalence and treatment differed from today. These characteristics likely result in overestimation of 30-year risk when using this tool in a younger, modern population.

Lifetime risk can be estimated using the ACC/AHA ASCVD Risk Estimator (https://tools.acc.org/ldl/ascvd_risk_estimator). This long-term calculator was based on a prior study that divided participants into five mutually exclusive sex-specific groups based on number of optimally controlled risk factors [29]. Thus, when one calculates lifetime risk using this tool, there are only five potential risk estimates that can be provided. Although a helpful construct for shared decision-making in patient care, lifetime risk estimation is somewhat limited in precision.

4.3 Risk Assessment in Elderly Populations

As life expectancy increases, there will be more opportunities for primary prevention in individuals greater than 75 years old. Unfortunately, the PCE has poor calibration and discrimination in this population and does not apply to individuals >79 years old. One study showed that in individuals >75 years old, the PCE

overestimates risk in the highest risk individuals, driven in part by competing risk of non-cardiovascular death [34]. Furthermore, the PCE does not address the risk of heart failure, and individuals >75 years old comprise 53% of heart failure hospitalizations [35]. A model developed for 4-year global CVD (incident CHD, stroke, and heart failure hospitalization) risk assessment that incorporated hs-cardiac troponin T, N-terminal pro-B-type natriuretic peptide, and hs-CRP was better able to discriminate high-risk from low-risk individuals compared to the standard PCE in an older population (mean age, 75.4 ± 5.1 years) [36]. Thus, the authors suggest that determining 35-year risk, as opposed to 10-year risk, and incorporating biomarkers indicative of subclinical injury, may provide more accurate risk assessment in elderly individuals.

5 Using Risk Enhancing Factors to Calibrate Risk Assessment

Calculating the Pooled Cohort Equations is the starting point of risk assessment. However, due to its limitations, additional factors can help guide the clinician patient risk discussion when treatment decisions are uncertain. These risk enhancing factors help inform risk prediction at the individual level and identify individuals at higher risk, who might otherwise not be captured by the PCE. The risk enhancing factors identified by the 2018 ACC/AHA Multi-society Guideline on the Management of Blood Cholesterol and the 2016 European Guidelines on Cardiovascular Disease Prevention in Clinical Practice are outlined in Table 1. Conceptually, risk enhancing factors can be divided into several categories: additional patient history, comorbid conditions, laboratory biomarkers, and imaging tests.

Several risk enhancing factors can be obtained from taking additional patient history. Family history of premature ASCVD (<55 years old in men, <65 years old in women) is readily ascertained in a patient visit and is associated with a higher risk of developing CVD [37, 38]. Offspring with at least one parent with premature CVD have an almost twofold increased risk of cardiovascular events, independent of traditional cardiovascular risk factors [38]. Family history of premature ASCVD improves risk prediction most in intermediate-risk individuals [38]. Several studies have demonstrated the incremental value of a positive family history of CVD, even in individuals with a CAC score of zero [39, 40].

South Asian ancestry is also a risk enhancing factor as studies have shown an increased risk for ASCVD in South Asians compared with other racial or ethnic groups [41, 42]. In a large study examining US death records from 2003 to 2010, Asian Indian men and women had a higher proportionate mortality burden for ischemic heart disease compared to non-Hispanic whites [42]. While the reasons for this increased risk are not completely elucidated, increased prevalence of insulin resistance and diabetes likely play a role. Further, the INTERHEART study

Table 1 Risk enhancing factors according to the 2018 ACC/AHA cholesterol guidelines and the 2016 European Guidelines on Cardiovascular Disease Prevention

	ACC/AHA[a]	ESC[b]
Family history of premature ASCVD	Males, age <55yo; females, age <65yo	Males, age <55yo; females, age <65yo
Metabolic syndrome	Increased waist circumference,[c] elevated triglycerides (>150 mg/dL, nonfasting), elevated BP, elevated glucose, low HDL-C (<40 mg/dL men, <50 mg/dL women). Tally of 3 makes the diagnosis.	Waist circumference >94 cm (men) or >80 cm (women); BMI target >20–25 kg/m^2
Primary hypercholesterolemia	LDL-C, 160–189 mg/dL, non-HDL 190–210 mg/dL	
Chronic kidney disease	eGFR 15–59 mL/min/1.73m^2, +/− albuminuria, not on dialysis or post kidney transplantation	
Chronic inflammatory conditions	For example, psoriasis, lupus, rheumatoid arthritis, HIV/AIDS	
Female-specific risk factors	Premature menopause (age <40 yo), pregnancy-associated condition that increases later ASCVD risk, such as preeclampsia	
High-risk race/ethnicity	For example, South Asian ancestry	
Biomarkers Triglycerides If measured: hs-CRP Lp(a) apo(B) ABI	Persistent elevated,[d] primary hypertriglyceridemia (≥175 mg/dL, nonfasting) ≥2.0 mg/L ≥50 mg/dL or ≥125 nmol/L[e] ≥130 mg/dL (corresponds to LDL-C >160 mg/dL) <0.9	Consider obtaining (IIb recommendation)
Socioeconomic status		Low socioeconomic status, lack of social support, stress, hostility, depression/anxiety
Atherosclerotic plaques determined by carotid artery screening		Consider obtaining (IIB recommendation)
Coronary artery calcium score		Consider obtaining (IIb recommendation)

[a]Adapted from the 2018 ACC/AHA Multi-society Guidelines on the Management of Blood Cholesterol

[b]Adapted from the 2016 European Guidelines on Cardiovascular Disease Prevention in Clinical Practice. The ESC guidelines recommend only six risk enhancing factors: family history, BMI/central obesity, ABI, socioeconomic status, carotid artery plaque, and coronary artery calcium score

[c]By ethnically appropriate cutoffs

[d]Optimally, three determinations

[e]Preferred units of measurement

demonstrated a similar importance of traditional risk factors for CHD in South Asians compared to other groups, but there was an increased prevalence of these risk factors at a younger age in the South Asian population [41, 43].

Risk enhancing factors specific to women include a history of premature menopause (<40 years old) and pregnancy complications known to increase ASCVD risk, such as preeclampsia [44–46]. The average age of menopause in the United States is approximately 50 years old. Both natural and surgical premature menopause are associated with an approximately two-fold increased risk of CHD after adjusting for traditional cardiovascular risk factors [47]. In a meta-analysis looking across a continuum of age of menopause, women younger than 45 years old at the onset had an almost 20% increased relative risk of CVD mortality compared to women who experienced menopause at 50 years old or older; this signal was not present for women 45–49 years at the age of menopause [48]. Recent literature has highlighted the association between pregnancy complications and future cardiovascular risk. Preeclampsia affects approximately 5 to 7% of all pregnancies in the United States [49]. Though there are variable findings between cohorts, overall, preeclampsia is associated with an almost twofold increase in CVD and an approximately threefold increased risk for developing hypertension [14, 50]. Other pregnancy complications such as preterm delivery (delivery at <32 weeks) also portend an increased risk of myocardial infarction and stroke [51]. Given the depth of evidence relating reproductive history and CVD, multiple society guidelines have emphasized the importance of taking a thorough reproductive history when assessing cardiovascular risk in women [14, 28, 52].

Comorbid inflammatory conditions such as psoriasis, rheumatoid arthritis, systemic lupus erythematosus (SLE), and HIV/AIDS are accompanied by an increased risk for CVD [53–55]. Rheumatologic conditions have been associated with increased cardiometabolic risk (defined as CHD, stroke, peripheral arterial disease, venous thromboembolism, and type 2 diabetes) as well as an increased risk of subclinical atherosclerosis [56]. This increased risk may be greater for SLE compared with psoriasis [57]. HIV-infected individuals have a 1.5–2-fold greater risk of myocardial infarction compared to noninfected individuals [58, 59]. This may be due to ~~an~~ more frequent hypertension, diabetes, and dyslipidemia in this population, some of which are known side effects of antiretroviral medications, or to adverse effects of the viremia itself [59]. Multivariable risk functions such as the Framingham Risk Score and PCE are poorly calibrated and underestimate risk in those with HIV [53].

Both the metabolic syndrome and chronic kidney disease are considered risk enhancing factors. The metabolic syndrome is defined as having three or more of the following: increased waist circumference, elevated triglycerides, low HDL, elevated blood pressure, and elevated fasting glucose. In a meta-analysis, metabolic syndrome is associated with an approximately 1.5–2-fold increase in CVD and CV mortality [60, 61]. Coronary artery disease is the leading cause of morbidity and mortality in individuals with chronic kidney disease, and risk for CVD mortality increases progressively with declining eGFR (HR 1.38, 95% CI 1.16–1.65, HR 2.42, 95% CI 1.92–3.05, and HR 3.29, 95% CI 1.72–6.31 for eGFR 45–59 mL/min/1.73 m^2, 30–44 mL/min/1.73 m^2, and 15–29 mL/min/1.73 m^2, respectively) [62, 63].

Several lipid parameters and biomarkers have also been identified as risk enhancing factors. C-reactive protein is an acute-phase reactant protein predominantly produced by the liver that is a nonspecific marker of systemic inflammation. Elevated levels of hs-CRP have consistently been associated with a range of CVD endpoints including an increased risk of CHD, ischemic stroke, and vascular death [64]. In the JUPITER trial of; individuals without CVD or hyperlipidemia (median LDL, 108 mg/dL), but elevated hs-CRP (median, 4.2 mg/L), rosuvastatin significantly reduced the incidence of major cardiovascular events compared with placebo [65]. Although interpretation of this trial is limited due to the lack of inclusion of individuals with normal hs-CRP levels, the results of this study and others suggest elevated hs-CRP may help identify those who derive benefit from statin therapy.

Lipoprotein(a) [Lp(a)] has a wealth of evidence regarding its role in identifying individuals at higher risk of CVD. Lp(a) is a low-density lipoprotein-like particle with an apolipoprotein-B100 (apoB_{100}) molecule linked to a large apolipoprotein(a) protein. Epidemiological [66], Mendelian randomization [67], and genome-wide association studies [68] have confirmed the causal association of elevated Lp(a) with a higher risk of CVD. Lp(a) is more atherogenic than LDL through its proatherogenic, pro-inflammatory, and antifibrinolytic properties [69]. The 2016 European Guidelines on Cardiovascular Disease Prevention and 2018 ACC/AHA Multi-society Guideline on the Management of Blood Cholesterol recommend an Lp(a) level ≥50 mg/dL (or ≥125 nmol/L) as the cutoff value for identifying individuals at greater risk for CVD.

Apolipoprotein(b) [apo(b)], persistently elevated triglycerides, and an ankle-brachial index (ABI) of <0.9 are additional parameters conveying ASCVD risk. Apolipoprotein(b)-100 is an apolipoprotein contained in atherogenic lipoprotein particles: LDL, IDL (intermediate-density lipoprotein), and VLDL (very-low-density lipoprotein). It is therefore an aggregate measure of these particles that has compared favorably to LDL-C in several studies. A large meta-analysis showed that apo(b) was a more potent marker of cardiovascular risk compared to both non-HDL-C and LDL-C [70]. Triglycerides persistently above 150 mg/dL are associated with increased risk for CHD and ischemic stroke, though this association is attenuated after adjusting for additional cardiac risk factors, specifically for HDL-C and non-HDL-C [71, 72]. Although less commonly measured in asymptomatic individuals, an ABI <0.9 is associated with a two-fold increase in MI and CV death and improves risk assessment beyond the Framingham Risk Score [73].

6 Alternative Tools for Risk Assessment

Although the Framingham Risk Score and Pooled Cohort Equations have been the most commonly used risk assessment tools in the United States, there are several other available risk calculators. These include models incorporating novel risk factors, those that have been developed in cohorts of different race/ethnicities and in cohorts outside of the United States. A summary of risk prediction tools, including the PCE, is presented in Table 2.

Table 2 Alternative tools for risk assessment

	Framingham	Pooled Cohort Equations (PCE)	Reynolds Risk Score	SCORE	ASSIGN	QRISK3	MESA Risk Score	Astro-CHARM
Population	Framingham, MA, USA. Baselines: 1968–71, 1971–75, 1984–87	ARIC, 1987–89; CHS 1990, 1992–1993 CARDIA, 1985–1986; FHS, 1968–1975, 1984–1987	WHS 1992–2004; PHS II 1995–2008	12 prospective studies from 11 European countries, 1972–1991	SHHEC Prospective Study, Scotland, 1984–1987	QRESEARCH database, UK, 1998–2015	MESA	MESA, DHS, PACC
Sample size	3969 men and 4522 women	11,240 white women, 9098 white men, 2641 African-American women, 1647 African-American men	10,724 men and 16,400 women	117,098 men and 88,080 women	6540 men and 6757 women	3.9 million men and 4.0 million women	3176 men and 3550 women	4060 men and 3322 women
Ethnicities represented	White	White, black	White, black, Hispanic, Asian (nonwhite <5%)	Not reported. 11/12 participating cohorts from Western Europe	White	White, black-Caribbean, black-African, South Asian, other Asian (nonwhite ~11%)	White, black, Hispanic, Chinese (nonwhite ~62%)	White, black, Hispanic
Calculates	10-year risk of CVD (2008) and 10-year risk of CHD (1998)	10-year risk for first atherosclerotic CVD event	10-year risk of CVD	10-year risk of CVD mortality (two versions for high- or low-risk countries)	10-year risk of CVD	10-year risk of CVD	10-year risk of CHD	10-year risk of ASCVD

Included endpoints	CVD: CHD, stroke, PAD, heart failure CHD: angina, MI, coronary insufficiency, CHD death	CHD death, nonfatal MI, fatal or nonfatal stroke	MI, stroke, coronary revascularization, CV death	CV mortality	CV death, CHD, cerebrovascular disease, CABG or PCI	CHD, ischemic stroke, TIA	MI, CHD death, resuscitated cardiac arrest, revascularization due to angina	CHD death, stroke death, nonfatal MI, nonfatal stroke
Age range (years)	30–75	40–79	48–58 (women); median 63 (men)	40–65	30–74	25–84	45–84	Mean age 51
Variables	Age, sex, total cholesterol, HDL-C, SBP, smoking, DM, hypertensive treatment	Age, sex, race (white/ African-American/other), total cholesterol, HDL-C, SBP, antihypertensive treatment, DM, smoking	Age, sex, total cholesterol, HDL-C, SBP, smoking, family history, hs-CRP	Age, sex, total cholesterol or total cholesterol/ HDL-C ratio, SBP, smoking	Age, sex, total cholesterol, HDL-C, SBP, quantitative smoking, DM, socioeconomic status, family history	Age, sex, ethnicity, total cholesterol/ HDL-C ratio, SBP, smoking, DM, socioeconomic status, family history, BMI, BP treatment and variability, chronic diseases	Age, sex, race (white, black, Hispanic, Chinese), total cholesterol, HDL-C, SBP, lipid-lowering med, BP medication, DM, smoking, family history, CAC	Age, sex, race (black/ Hispanic/ other), total cholesterol, HDL-C, SBP, BP medication, smoking, DM, family history, hs-CRP, CAC score

Based on data from the ESC 2016 Primary Prevention of Cardiovascular Disease Guidelines

ARIC Atherosclerosis Risk in Communities, *CARDIA* Coronary Artery Risk Development in Young Adults, *FHS* Framingham Heart Study, *WHS* Women's Health Study, *PHS II* Physician's Health Study II, *SHHEC* Scottish Heart Health Extended Cohort, *MESA* Multi-Ethnic Study of Atherosclerosis, *DHS* Dallas Heart Study, *PACC* Prospective Army Coronary Calcium Project, *CVD* cardiovascular disease, *CHD* coronary heart disease, *TIA* transient ischemic attack, *DM* diabetes mellitus, *BMI* body mass index

Utilizing a tool derived from a population most representative of the patient being assessed will provide more accurate risk assessment. The Systematic COronary Risk Evaluation (SCORE) project was undertaken to develop a risk assessment tool specifically for use in European clinical practice [74]. SCORE was derived from 12 cohorts from Western Europe and Russia. Unlike other risk assessment tools, its defined endpoint is total cardiovascular mortality. This departure is notable for only CVD mortality instead of including nonfatal events. This decision was based on the lack of ascertainment of nonfatal CVD endpoints in the derivation cohorts. A multiplier has been recommended to estimate risk of nonfatal CVD events [52]. SCORE data indicate that the rate of total CVD is three times higher than fatal CVD for men, four times higher for women, and somewhat lower than 3 for the elderly [52]. Compared to other risk assessment tools, SCORE includes a relatively narrow list of risk factors in its model: cholesterol and HDL levels, sex, smoking status, and systolic blood pressure. Importantly, it does include diabetes as a factor and defines all such persons at high or very high risk. However, the guidelines recommend considering other cardiovascular risk factors, such as premature family history and an elevated CAC score, when using this tool in clinical practice [52]. SCORE is ~~to~~ recommended for use throughout Europe. As such, there are two SCORE calculators – one for use in countries with baseline low risk of CVD and another for countries with a baseline high risk of CVD.

Several risk scores have been developed which incorporate novel risk factors, some of which are risk enhancing factors, into their models. The Reynolds Risk Score incorporates hs-CRP as well as family history into its risk assessment algorithms. The Reynolds Risk Score for women was derived and validated using data from the Women's Health Study, and a similar score for men, the Reynolds Risk Score for men, was derived and validated using data from the Physicians Health Study [11, 12]. The Reynolds Risk Score for women has improved calibration and discrimination compared to the Framingham Risk Score for CHD [11]. While family history is readily ascertained in a standard patient visit, the Reynolds Risk Score is limited by its reliance on hs-CRP, which is not routinely obtained.

The ASSIGN score was developed in 2006 from the Scottish Heart Health Extended Cohort (SHHEC) [27]. In addition to traditional cardiovascular risk factors, ASSIGN incorporates family history, quantitative measures of cigarette smoking (i.e., amount smoked), and social deprivation according to the Scottish Index of Multiple Deprivation. The ASSIGN score had marginally better discrimination and improved calibration compared to the Framingham Risk Score. However, it is limited by the homogenous population in which it was derived and its incorporation of additional risk factors such as social deprivation which vary in ascertainment between regions.

QRISK, initially developed in 2007, built off these previous scores by incorporating additional novel risk factors. The QRISK score was developed using the QRESEARCH database, consisting exclusively of practices in the United Kingdom [13]. Similar to ASSIGN, it added social deprivation and family history into its model, as well as body mass index (BMI). Since the initial development of QRISK, there have been two additional iterations of the model: QRISK2 and QRISK3.

QRISK2 added self-described ethnicity (divided into nine possible groups), rheumatoid arthritis, chronic renal disease, type 2 diabetes, and atrial fibrillation to the model [75]. The latest version, QRISK3, added systolic blood pressure variability, migraine history, steroid and antipsychotic use, severe mental illness, history of lupus, and erectile dysfunction [76]. The original QRISK score has improved discrimination and calibration compared to the Framingham Risk Score and ASSIGN and has been validated in another UK cohort [77]. However, QRISK scores have not been validated in a non-European cohort. Though ethnicity factored into QRISK2 and QRISK3, >95% of the derivation and validation cohorts were white. The QRISK scores also require inputting multiple risk factors, some of which may not be readily available in routine clinical practice, hindering their ease of use. Lastly, there was no formal adjudication of events in the QRISK cohort, possibly limiting its accuracy. A QRISK lifetime risk calculator is also available [52, 78].

Since a difference in baseline cardiovascular risk exists between countries and individuals of different ethnicity and race, the GLOBORISK score was developed as a tool for risk assessment that could be calibrated to many different countries worldwide [79]. The score was derived using eight cohorts (ARIC, CHS, FHS Original and Offspring, WHI, Honolulu Heart Program, Multiple Risk Factor Intervention Trial, Puerto Rico Heart Health Program), with six out of the eight cohorts being from the United States, one of Japanese Americans from Hawaii (Honolulu Heart Program), and the last consisting of Puerto Rican men. It was then validated in cohorts outside of the United States: the Scottish Heart Health Extended Cohort, Tehran Lipid and Glucose Study, and the Australian Diabetes, Obesity, and Lifestyle cohort. The resulting tool is a series of charts, similar to the SCORE model, that are specific for a given country, with primary outcome of fatal ASCVD. The model showed good discrimination in internal and external validation and also demonstrated that risk varied substantially between high-, middle-, and low-income countries. To facilitate use, in addition to risk assessment charts that use lab-based information (i.e., total cholesterol), there are also ones using only data that can be obtained in the office (i.e., blood pressure and BMI). While the authors focused on fatal ASCVD (i.e., CHD and stroke), they also developed scores for fatal and nonfatal ASCVD but only for those countries that had high-quality data for those outcomes. There are currently 182 country risk charts available for use and may be beneficial for those practicing in other countries or populations without representative risk equations (www.globorisk.org).

Coronary artery calcium scores are perhaps the strongest predictors of ASCVD risk [80–82]. A simplified approach to incorporating CAC scores in risk assessment is using low or elevated (i.e., >0 vs. ≥100) scores to dichotomously identify individuals at lower or higher risk. However, CAC scores, and thereby associated risk, exist on a continuum and simplified methods using categorical thresholds result in imprecise risk prediction. Novel risk calculators include continuous CAC scores and are potentially valuable tools to help refine risk assessment.

The MESA risk score incorporates CAC scores, as well as family history, to estimate 10-year CHD risk, including myocardial infarction, resuscitated cardiac arrest, fatal CHD, and revascularization for angina [83]. It was derived from a

multiethnic cohort including Chinese-, African-, and Hispanic-Americans and was validated in two external cohorts, the Heinz Nixdorf Recall Study (HNR) and the Dallas Heart Study (DHS). Compared to the score without CAC, the addition of CAC showed improved discrimination and calibration.

The Astro-CHARM risk prediction tool expands from the MESA findings and incorporates CAC scores to estimate 10-year hard ASCVD risk, similar to the PCE endpoint [84]. Astro-CHARM was developed using the MESA, DHS, and Prospective Army Coronary Calcium Project (PACC) cohorts, all of which comprise of black, white, and Hispanic participants, and was externally validated in the Framingham Heart Study cohorts. In addition to CAC and family history, hs-CRP was also added to the final risk prediction model. Similar to the MESA risk score, the final model improved discrimination, calibration, and risk classification compared to the one comprising only ~~of~~ traditional risk factors. Both the MESA (www.mesa-nhlbi.org/MESACHDRisk) and Astro-CHARM (www.astrocharm.org) models are available as online tools.

7 Risk Factors Not Represented in Risk Assessment Tools

Other risk factors have not been incorporated into risk prediction tools, despite their known contribution to the development of ASCVD, due to difficulty with quantification or lack of improvement in discrimination when they were added to traditional risk assessment models, including the PCE [10]. These risk factors include diet, physical activity, and obesity [8].

Optimal dietary patterns, such as the DASH or Mediterranean diet, include high intake of fruits, vegetables, and whole grains and are low in saturated fats, meats, and higher fat dairy products. Poor dietary patterns have been associated with an increased risk of developing cardiovascular risk factors and myocardial infarction [85, 86]. Similarly, physical inactivity and poor cardiorespiratory fitness correlate with a worse cardiometabolic biomarker profile and increased risk for CVD [87–91]. Nevertheless, despite independent association of diet and physical activity with CVD outcomes, these parameters do not seem to add incremental information to risk prediction beyond PCE factors [92].

Obesity is independently associated with an increased risk of cardiovascular disease [93, 94]. However, the concept of "metabolically healthy obesity" (MHO) has emerged. Debate exists on whether these individuals who are obese but do not have features of the metabolic syndrome have increased risk of CVD [95]. These individuals tend to be younger, of non-Hispanic or black ethnicity, physically active, have higher cardiorespiratory fitness levels, and have lower levels of abdominal visceral adipose tissue or ectopic fat [96]. Different studies use varying combinations of elevated blood pressure, low HDL, high triglycerides, and elevated fasting glucose to define MHO. This has led to conflicting results in the literature. However, large meta-analyses show that compared to metabolically healthy, normal BMI individuals, those who are overweight, obese, or metabolically unhealthy regardless of

their weight had a higher risk of CVD especially in the long term, suggesting that MHO exists on a spectrum and these individuals are on the path for developing CVD risk factors [96, 97]. When evaluating obesity parameters, waist circumference is a better measure of metabolically active intra-abdominal adipose tissue and should be assessed to identify those at higher cardiometabolic risk [28]. Interestingly, addition of BMI to the model did not improve risk prediction in PCE model development. Notably, BMI and waist circumference have been incorporated into the QRISK scores [76].

Across the entire spectrum of age, those who have optimal lifestyle habits have a lower risk for CVD [98–100]. While lifestyle factors may not incrementally inform ASCVD risk estimates, they remain important modifiable targets to lower the risk of developing ASCVD. Assessing for the presence of a healthy lifestyle pattern should be included in routine risk assessment.

8 Summary of the ACC/AHA and ESC Guidelines

The American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology (ESC) have each made recommendations on risk assessment for primary prevention.

8.1 ACC/AHA 2019 Primary Prevention Guidelines

The starting point for primary prevention begins with global risk scoring. Foundational to this is assessment for a heart-healthy lifestyle and counseling the patient on lifestyle interventions as needed, as part of the clinician-patient discussion on the best ways to reduce CVD risk. The guidelines recommend routine assessment for 10-year risk of ASCVD in asymptomatic 40–75-year-olds free of CVD using the PCE [28]. No specific time interval was provided for the frequency of this assessment. Risk assessment should be the starting point for the physician-patient conversation and not the sole factor in the decision to initiate preventive therapies. For blood pressure management, individuals with blood pressure of 130–139/80–89 mmHg with 10-year ASCVD risk estimated to be ≥10% would benefit from therapies to reduce their blood pressure to a goal of <130/80 mmHg. Similarly, those with blood pressure ≥140/90 mmHg are recommended antihypertensive therapy regardless of ASCVD risk. With regards to blood cholesterol management, individuals whose 10-year risk is greater than 20% are deemed high risk and aggressive risk modification is recommended, including reduction in LDL-C levels by 50% or more. Those whose risk is between 7.5 and 20% are at intermediate risk, and individuals whose 10-year risk is between 5 and <7.5% are borderline risk. For individuals at borderline or intermediate risk, the presence of risk enhancing factors favors initiation or intensification of statin therapy. If the patient's overall risk

still remains in question and/or the physician or patient is uncertain about initiating preventive therapies, CAC scanning can further guide the risk discussion, with scores of 0 favoring deferral of statin therapy (as long as diabetes, cigarette smoking, or a premature family history of ASCVD is not present) and scores of ≥100 or ≥75th percentile favoring initiation. Both the MESA CAC risk score and Astro-CHARM are mentioned as options to integrate CAC values with traditional risk factors for quantitative risk estimates in the 2019 ACC/AHA Prevention Guidelines. A statin treatment algorithm according to the 2018 ACC/AHA cholesterol guidelines is outlined in Fig. 3.

For younger individuals (20–39 years old), assessment of traditional ASCVD risk factors every 4–6 years is recommended. Global risk prediction in this population using either 30-year or lifetime risk assessment tools can be considered. For individuals >75 years old, a patient-physician discussion on the risks and benefits of preventive therapies in the context of possible other comorbidities and life expectancy is an appropriate starting point.

8.2 ESC 2016 Cardiovascular Disease Prevention Guidelines

While the European guidelines agree that assessment of global cardiovascular risk is indicated, and that treatment should be commensurate to the degree of risk, it differs from the American recommendations in whom and when to assess risk. The ESC guidelines recommend risk assessment in individuals with risk factors or comorbidities increasing cardiovascular risk (i.e., family history of premature disease or the presence of major cardiovascular risk factors) [52]. Furthermore, risk assessment is recommended every 5 years though can be more frequent in those individuals nearing the higher-risk thresholds. Lastly, risk assessment in younger individuals (men <40 and women <50 years old) with no known cardiovascular risk factors is not recommended.

For those in whom risk assessment is recommended, the European guidelines recommend using SCORE to assess risk of cardiovascular death. Practitioners in Europe should use either the low- or high-cardiovascular risk calculator depending on the country in which he or she practices. Similar to the ACC/AHA guidelines, the European guidelines recommend that risk calculation should start the physician-patient discussion regarding preventive therapies but not be the absolute determinant of medication initiation.

Notably, the ESC cutoffs for the definition of high-, moderate-, and low-risk individuals vary from those of the ACC/AHA, since the ESC SCORE endpoint is CVD mortality. Very high-risk individuals have an absolute 10-year risk of >10% and drug therapies are recommended. For high-risk (5–10%) individuals, drug therapy can be considered but focus should be paid to intensifying lifestyle interventions. Low- to moderate-risk (<5%) individuals should be counseled on lifestyle interventions. For individuals at the borderline of risk (>5%), the presence of risk modifiers can be considered to classify a patient's risk upward. It is worth noting that risk modifiers in the European guidelines differ slightly from those in the ACC/AHA guidelines (Table 1).

For younger individuals (defined as <50 years old) with a family history of premature CVD, assessing for familial hypercholesterolemia or the presence of cardiovascular risk factors is recommended. Assessment of relative risk or lifetime risk can be considered, but the guidelines conclude that in the absence of very high individual risk factors, cholesterol-lowering or blood pressure therapy is rarely indicated in a younger population. Global risk assessment in elderly individuals is not recommended due to the lack of definitive evidence for primary prevention in this group, as well as the competing risk for non-cardiovascular disease. As with the ACC/AHA guidelines, a physician-patient discussion regarding risks/benefits of therapy, quality of life, and burden of drug treatment is recommended in this population.

9 Conclusion

Primary prevention of cardiovascular disease begins with determining an individual's global, absolute, short-term (10-year) risk for atherosclerotic CVD. Risk enhancing factors should also be considered to calibrate a patient's risk either upward or downward. Global risk assessment, supplemented by the consideration

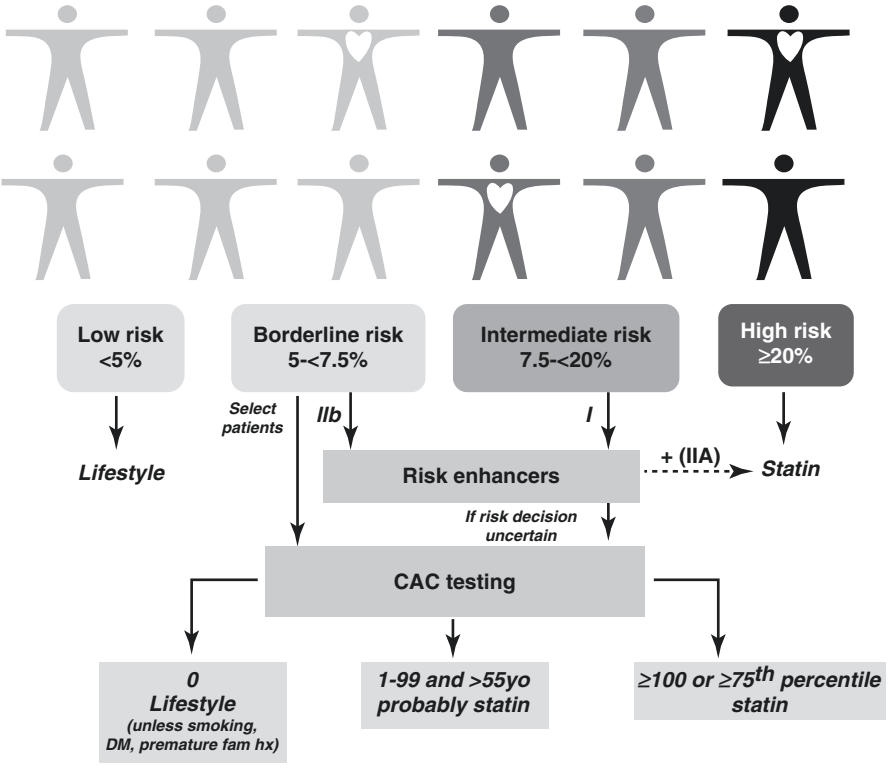

Fig. 3 Statin treatment algorithm according to the 2018 ACC/AHA cholesterol guidelines

of risk enhancing factors and where necessary coronary calcium measures, should inform the physician-patient discussion on the risks and benefits of starting preventive therapies. The intensity of preventive therapies should be commensurate to the degree of risk, with the highest-risk individuals receiving the most intensive treatment. Finally, practitioners should be aware of the shortcomings of all risk assessment tools and factor these into their final conclusions or recommendations.

References

1. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. Circulation. 2019;139:e56–e528.
2. Rose G. Sick individuals and sick populations. Int J Epidemiol. 1985;14:32–8.
3. Califf RM, Armstrong PW, Carver JR, et al. 27th Bethesda conference: matching the intensity of risk factor management with the hazard for coronary disease events. Task Force 5. Stratification of patients into high, medium and low risk subgroups for purposes of risk factor management. J Am Coll Cardiol. 1996;27:1007–19.
4. National Cholesterol Education Program Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. Circulation. 2002;106:3143–421.
5. Furberg CD, Hennekens CH, Hulley SB, et al. 27th Bethesda conference: matching the intensity of risk factor management with the hazard for coronary disease events. Task Force 2. Clinical epidemiology: the conceptual basis for interpreting risk factors. J Am Coll Cardiol. 1996;27:976–8.
6. Kannel WB, Dawber TR, Kagan A, et al. Factors of risk in the development of coronary heart disease--six year follow-up experience. The Framingham Study. Ann Intern Med. 1961;55:33–50.
7. Gordon T, Kannel WB. Multiple risk functions for predicting coronary heart disease: the concept, accuracy, and application. Am Heart J. 1982;103:1031–9.
8. Wilson PW, D'Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. Circulation. 1998;97:1837–47.
9. D'Agostino RB Sr, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117:743–53.
10. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129:S49–73.
11. Ridker PM, Buring JE, Rifai N, et al. Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds Risk Score. JAMA. 2007;297:611–9.
12. Ridker PM, Paynter NP, Rifai N, et al. C-reactive protein and parental history improve global cardiovascular risk prediction: the Reynolds Risk Score for men. Circulation. 2008;118:2243–51, 4p following 2251
13. Hippisley-Cox J, Coupland C, Vinogradova Y, et al. Derivation and validation of QRISK, a new cardiovascular disease risk score for the United Kingdom: prospective open cohort study. BMJ. 2007;335:136.
14. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139:e1046–81.

15. Muntner P, Colantonio LD, Cushman M, et al. Validation of the atherosclerotic cardiovascular disease Pooled Cohort risk equations. JAMA. 2014;311:1406–15.
16. Pursnani A, Massaro JM, D'Agostino RB, et al. Guideline-based statin eligibility, coronary artery calcification, and cardiovascular events. JAMA. 2015;314:134–41.
17. Rana JS, Tabada GH, Solomon MD, et al. Accuracy of the atherosclerotic cardiovascular risk equation in a large contemporary, multiethnic population. J Am Coll Cardiol. 2016;67:2118–30.
18. Ridker PM, Cook NR. Statins: new American guidelines for prevention of cardiovascular disease. Lancet. 2013;382:1762–5.
19. Kavousi M, Leening MJ, Nanchen D, et al. Comparison of application of the ACC/AHA guidelines, Adult Treatment Panel III guidelines, and European Society of Cardiology guidelines for cardiovascular disease prevention in a European cohort. JAMA. 2014;311:1416–23.
20. DeFilippis AP, Young R, Carrubba CJ, et al. An analysis of calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort. Ann Intern Med. 2015;162:266–75.
21. Pylypchuk R, Wells S, Kerr A, et al. Cardiovascular disease risk prediction equations in 400 000 primary care patients in New Zealand: a derivation and validation study. Lancet. 2018;391:1897–907.
22. Jung KJ, Jang Y, Oh DJ, et al. The ACC/AHA 2013 pooled cohort equations compared to a Korean Risk Prediction Model for atherosclerotic cardiovascular disease. Atherosclerosis. 2015;242:367–75.
23. Yang X, Li J, Hu D, et al. Predicting the 10-year risks of atherosclerotic cardiovascular disease in Chinese population: the China-PAR project (prediction for ASCVD risk in China). Circulation. 2016;134:1430–40.
24. DeFilippis AP, Young R, McEvoy JW, et al. Risk score overestimation: the impact of individual cardiovascular risk factors and preventive therapies on the performance of the American Heart Association-American College of Cardiology-Atherosclerotic Cardiovascular Disease risk score in a modern multi-ethnic cohort. Eur Heart J. 2017;38:598–608.
25. Colantonio LD, Richman JS, Carson AP, et al. Performance of the atherosclerotic cardiovascular disease pooled cohort risk equations by social deprivation status. J Am Heart Assoc. 2017;6(3):e005676.
26. Dalton JE, Perzynski AT, Zidar DA, et al. Accuracy of cardiovascular risk prediction varies by neighborhood socioeconomic position: a retrospective cohort study. Ann Intern Med. 2017;167:456–64.
27. Woodward M, Brindle P, Tunstall-Pedoe H, et al. Adding social deprivation and family history to cardiovascular risk assessment: the ASSIGN score from the Scottish Heart Health Extended Cohort (SHHEC). Heart. 2007;93:172–6.
28. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;140:e596–646.
29. Lloyd-Jones DM, Leip EP, Larson MG, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. Circulation. 2006;113:791–8.
30. Berry JD, Dyer A, Cai X, et al. Lifetime risks of cardiovascular disease. N Engl J Med. 2012;366:321–9.
31. Wilkins JT, Ning H, Berry J, et al. Lifetime risk and years lived free of total cardiovascular disease. JAMA. 2012;308:1795–801.
32. Berry JD, Liu K, Folsom AR, et al. Prevalence and progression of subclinical atherosclerosis in younger adults with low short-term but high lifetime estimated risk for cardiovascular disease: the coronary artery risk development in young adults study and multi-ethnic study of atherosclerosis. Circulation. 2009;119:382–9.
33. Pencina MJ, D'Agostino RB Sr, Larson MG, et al. Predicting the 30-year risk of cardiovascular disease: the Framingham Heart Study. Circulation. 2009;119:3078–84.

34. Nanna MD, Peterson ED, Wojdyla D, et al. The accuracy of cardiovascular pooled cohort risk estimates in U.S. older adults. J Gen Intern Med. 2020;35(6):1701–8.
35. Hall MJ, Levant S, DeFrances CJ. Hospitalization for congestive heart failure: United States, 2000-2010. NCHS Data Brief. 2012;(108):1–8.
36. Saeed A, Nambi V, Sun W, et al. Short-term global cardiovascular disease risk prediction in older adults. J Am Coll Cardiol. 2018;71:2527–36.
37. Seshadri S, Beiser A, Pikula A, et al. Parental occurrence of stroke and risk of stroke in their children: the Framingham study. Circulation. 2010;121:1304–12.
38. Lloyd-Jones DM, Nam BH, D'Agostino RB Sr, et al. Parental cardiovascular disease as a risk factor for cardiovascular disease in middle-aged adults: a prospective study of parents and offspring. JAMA. 2004;291:2204–11.
39. Paixao AR, Berry JD, Neeland IJ, et al. Coronary artery calcification and family history of myocardial infarction in the Dallas heart study. JACC Cardiovasc Imaging. 2014;7:679–86.
40. Cohen R, Budoff M, McClelland RL, et al. Significance of a positive family history for coronary heart disease in patients with a zero coronary artery calcium score (from the Multi-Ethnic Study of Atherosclerosis). Am J Cardiol. 2014;114:1210–4.
41. Volgman AS, Palaniappan LS, Aggarwal NT, et al. Atherosclerotic cardiovascular disease in South Asians in the United States: epidemiology, risk factors, and treatments: a scientific statement from the American Heart Association. Circulation. 2018;138:e1–e34.
42. Jose PO, Frank AT, Kapphahn KI, et al. Cardiovascular disease mortality in Asian Americans. J Am Coll Cardiol. 2014;64:2486–94.
43. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. JAMA. 2007;297:286–94.
44. Honigberg MC, Zekavat SM, Aragam K, et al. Association of premature natural and surgical menopause with incident cardiovascular disease. JAMA. 2019;322(24):2411–21.
45. Riise HK, Sulo G, Tell GS, et al. Incident coronary heart disease after preeclampsia: role of reduced fetal growth, preterm delivery, and parity. J Am Heart Assoc. 2017;6(3):e004158.
46. Wu P, Haththotuwa R, Kwok CS, et al. Preeclampsia and future cardiovascular health: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes. 2017;10(2):e003497.
47. Wellons M, Ouyang P, Schreiner PJ, et al. Early menopause predicts future coronary heart disease and stroke: the Multi-Ethnic Study of Atherosclerosis. Menopause. 2012;19:1081–7.
48. Muka T, Oliver-Williams C, Kunutsor S, et al. Association of age at onset of menopause and time since onset of menopause with cardiovascular outcomes, intermediate vascular traits, and all-cause mortality: a systematic review and meta-analysis. JAMA Cardiol. 2016;1:767–76.
49. Rana S, Lemoine E, Granger JP, et al. Preeclampsia: pathophysiology, challenges, and perspectives. Circ Res. 2019;124:1094–112.
50. Ahmed R, Dunford J, Mehran R, et al. Pre-eclampsia and future cardiovascular risk among women: a review. J Am Coll Cardiol. 2014;63:1815–22.
51. Tanz LJ, Stuart JJ, Williams PL, et al. Preterm delivery and maternal cardiovascular disease in young and middle-aged adult women. Circulation. 2017;135:578–89.
52. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J. 2016;37:2315–81.
53. Triant VA, Perez J, Regan S, et al. Cardiovascular risk prediction functions underestimate risk in HIV infection. Circulation. 2018;137:2203–14.
54. del Rincon ID, Williams K, Stern MP, et al. High incidence of cardiovascular events in a rheumatoid arthritis cohort not explained by traditional cardiac risk factors. Arthritis Rheum. 2001;44:2737–45.
55. Manzi S, Meilahn EN, Rairie JE, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol. 1997;145:408–15.

56. Asanuma Y, Oeser A, Shintani AK, et al. Premature coronary-artery atherosclerosis in systemic lupus erythematosus. N Engl J Med. 2003;349:2407–15.
57. Dregan A, Chowienczyk P, Molokhia M. Cardiovascular and type 2 diabetes morbidity and all-cause mortality among diverse chronic inflammatory disorders. Heart. 2017;103:1867–73.
58. Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. JAMA Intern Med. 2013;173:614–22.
59. Triant VA, Lee H, Hadigan C, et al. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab. 2007;92:2506–12.
60. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. J Am Coll Cardiol. 2010;56:1113–32.
61. Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol. 2007;49:403–14.
62. Chronic Kidney Disease Prognosis Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet. 2010;375:2073–81.
63. Sarnak MJ, Amann K, Bangalore S, et al. Chronic kidney disease and coronary artery disease: JACC state-of-the-art review. J Am Coll Cardiol. 2019;74:1823–38.
64. Emerging Risk Factors Collaborative. C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: an individual participant meta-analysis. Lancet. 2010;375:132–40.
65. Ridker PM, Danielson E, Fonseca FA, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med. 2008;359:2195–207.
66. Emerging Risk Factors Collaborative. Lipoprotein(a) concentration and the risk of coronary heart disease, stroke, and nonvascular mortality. JAMA. 2009;302:412–23.
67. Kamstrup PR, Tybjaerg-Hansen A, Nordestgaard BG. Extreme lipoprotein(a) levels and improved cardiovascular risk prediction. J Am Coll Cardiol. 2013;61:1146–56.
68. Clarke R, Peden JF, Hopewell JC, et al. Genetic variants associated with Lp(a) lipoprotein level and coronary disease. N Engl J Med. 2009;361:2518–28.
69. Tsimikas S. A test in context: lipoprotein(a): diagnosis, prognosis, controversies, and emerging therapies. J Am Coll Cardiol. 2017;69:692–711.
70. Sniderman AD, Williams K, Contois JH, et al. A meta-analysis of low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and apolipoprotein B as markers of cardiovascular risk. Circ Cardiovasc Qual Outcomes. 2011;4:337–45.
71. Emerging Risk Factors Collaborative. Major lipids, apolipoproteins, and risk of vascular disease. JAMA. 2009;302:1993–2000.
72. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk. 1996;3:213–9.
73. Ankle Brachial Index Collaboration. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA. 2008;300:197–208.
74. Conroy RM, Pyorala K, Fitzgerald AP, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J. 2003;24:987–1003.
75. Hippisley-Cox J, Coupland C, Vinogradova Y, et al. Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2. BMJ. 2008;336:1475–82.
76. Hippisley-Cox J, Coupland C, Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. BMJ. 2017;357:j2099.
77. Hippisley-Cox J, Coupland C, Vinogradova Y, et al. Performance of the QRISK cardiovascular risk prediction algorithm in an independent UK sample of patients from general practice: a validation study. Heart. 2008;94:34–9.

78. Hippisley-Cox J, Coupland C, Robson J, et al. Derivation, validation, and evaluation of a new QRISK model to estimate lifetime risk of cardiovascular disease: cohort study using QResearch database. BMJ. 2010;341:c6624.
79. Hajifathalian K, Ueda P, Lu Y, et al. A novel risk score to predict cardiovascular disease risk in national populations (Globorisk): a pooled analysis of prospective cohorts and health examination surveys. Lancet Diabetes Endocrinol. 2015;3:339–55.
80. Carr JJ, Jacobs DR Jr, Terry JG, et al. Association of coronary artery calcium in adults aged 32 to 46 years with incident coronary heart disease and death. JAMA Cardiol. 2017;2:391–9.
81. Budoff MJ, Young R, Burke G, et al. Ten-year association of coronary artery calcium with atherosclerotic cardiovascular disease (ASCVD) events: the multi-ethnic study of atherosclerosis (MESA). Eur Heart J. 2018;39:2401–8.
82. Mahabadi AA, Mohlenkamp S, Lehmann N, et al. CAC score improves coronary and CV risk assessment above statin indication by ESC and AHA/ACC primary prevention guidelines. JACC Cardiovasc Imaging. 2017;10:143–53.
83. McClelland RL, Jorgensen NW, Budoff M, et al. 10-Year coronary heart disease risk prediction using coronary artery calcium and traditional risk factors: derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) with validation in the HNR (Heinz Nixdorf Recall) Study and the DHS (Dallas Heart Study). J Am Coll Cardiol. 2015;66:1643–53.
84. Khera A, Budoff MJ, O'Donnell CJ, et al. Astronaut cardiovascular health and risk modification (Astro-CHARM) coronary calcium atherosclerotic cardiovascular disease risk calculator. Circulation. 2018;138:1819–27.
85. Anand SS, Hawkes C, de Souza RJ, et al. Food consumption and its impact on cardiovascular disease: importance of solutions focused on the globalized food system: a report from the workshop convened by the world heart federation. J Am Coll Cardiol. 2015;66:1590–614.
86. Iqbal R, Anand S, Ounpuu S, et al. Dietary patterns and the risk of acute myocardial infarction in 52 countries: results of the INTERHEART study. Circulation. 2008;118:1929–37.
87. Lavie CJ, Ozemek C, Carbone S, et al. Sedentary behavior, exercise, and cardiovascular health. Circ Res. 2019;124:799–815.
88. Lee IM, Shiroma EJ, Lobelo F, et al. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet. 2012;380:219–29.
89. Shiroma EJ, Lee IM. Physical activity and cardiovascular health: lessons learned from epidemiological studies across age, gender, and race/ethnicity. Circulation. 2010;122:743–52.
90. Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA. 2009;301:2024–35.
91. Healy GN, Matthews CE, Dunstan DW, et al. Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003-06. Eur Heart J. 2011;32:590–7.
92. Paynter NP, LaMonte MJ, Manson JE, et al. Comparison of lifestyle-based and traditional cardiovascular disease prediction in a multiethnic cohort of nonsmoking women. Circulation. 2014;130:1466–73.
93. Wilson PW, D'Agostino RB, Sullivan L, et al. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. Arch Intern Med. 2002;162:1867–72.
94. Khan SS, Ning H, Wilkins JT, et al. Association of Body Mass Index with lifetime risk of cardiovascular disease and compression of morbidity. JAMA Cardiol. 2018;3:280–7.
95. Despres JP. Body fat distribution and risk of cardiovascular disease: an update. Circulation. 2012;126:1301–13.
96. Neeland IJ, Poirier P, Despres JP. Cardiovascular and metabolic heterogeneity of obesity: clinical challenges and implications for management. Circulation. 2018;137:1391–406.
97. Eckel N, Meidtner K, Kalle-Uhlmann T, et al. Metabolically healthy obesity and cardiovascular events: a systematic review and meta-analysis. Eur J Prev Cardiol. 2016;23:956–66.
98. Knoops KT, de Groot LC, Kromhout D, et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. JAMA. 2004;292:1433–9.

99. Stampfer MJ, Hu FB, Manson JE, et al. Primary prevention of coronary heart disease in women through diet and lifestyle. N Engl J Med. 2000;343:16–22.
100. Gooding HC, Ning H, Gillman MW, et al. Application of a lifestyle-based tool to estimate premature cardiovascular disease events in Young adults: the coronary artery risk development in young adults (CARDIA) study. JAMA Intern Med. 2017;177:1354–60.
101. Jackson R, Lawes CM, Bennett DA, Milne RJ, Rodgers A. Treatment with drugs to lower blood pressure and blood cholesterol based on an individual's absolute cardiovascular risk. Lancet. 2005;365:434–41.
102. Khera A. History of the evolution of cardiovascular risk factors and the predictive value of traditional risk factor-based risk assessment. In: Naghavi M, editor. Asymptomatic atherosclerosis: pathophysiology, detection, and treatment. Surrey: Humana Press; 2009. p. 89–105.

Assessment and Management of Psychosocial Risk Factors Within Preventive Cardiology Practice

Alan Rozanski

Summary

- Traditional psychosocial factors associated with cardiovascular disease (CVD) include depression, anxiety, social isolation or poor social support, hostility, and chronic stress.
- Increasing data also points to a significant association between CVD and pessimism, low sense of life purpose, and vital exhaustion.
- A gradient relationship has been demonstrated between the magnitude of these negative risk factors and CVD risk.
- Positive factors, such as optimism and high sense of life purpose, appear to be associated with enhanced survival and decreased CVD risk.
- Two general pathophysiological mechanisms may link psychosocial risk factors to CVD: direct pathophysiological effects and their negative impact on health behaviors (e.g., more likely to smoke, be sedentary, and eat poorly).
- Cardiologists can help manage psychosocial risk factors by screening for their presence and then either managing these factors in some cases, referring patients to hospital- or community-based programs, or referring patients with more severe psychosocial dysfunction to mental health professionals.

A. Rozanski (✉)
Department of Cardiology, Mount Sinai Morningside Hospital and Mount Sinai Heart, Icahn School of Medicine at Mount Sinai, New York, NY, USA
e-mail: Alan.Rozanski@mountsinai.org

N. D. Wong et al. (eds.), *ASPC Manual of Preventive Cardiology*,
Contemporary Cardiology, https://doi.org/10.1007/978-3-030-56279-3_4