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THE PRESENT AND FUTURE

JACC COUNCIL PERSPECTIVES

Preventive Cardiology as a Subspecialty of Cardiovascular Medicine

JACC Council Perspectives

Michael D. Shapiro, DO, MCR,[a] David J. Maron, MD,[b] Pamela B. Morris, MD,[c] Mikhail Kosiborod, MD,[d,e] Pratik B. Sandesara, MD,[f] Salim S. Virani, MD, PhD,[g] Amit Khera, MD, MSc,[h] Christie M. Ballantyne, MD,[i] Seth J. Baum, MD,[j] Laurence S. Sperling, MD,[k] Deepak L. Bhatt, MD, MPH,[l] Sergio Fazio, MD, PhD[m]

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CME/MOC/ECME Objective for This Article: Upon completion of this activity, the learner should be able to: 1) discuss the coalescence of competencies necessary to provide expert guidance to patients seeking cardiovascular risk assessment and management; and 2) define initial strategies to consolidate and standardize education and training in cardiovascular disease prevention.

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From the [a]Center for Preventive Cardiology, Section on Cardiovascular Medicine, Wake Forest University Baptist Medical Center, Winston-Salem, North Carolina; [b]Department of Medicine and Cardiovascular Institute, Stanford University, Stanford, California; [c]Seinsheimer Cardiovascular Health Program, The Medical University of South Carolina, Charleston, South Carolina; [d]Saint Luke's Mid America Heart Institute and University of Missouri-Kansas City, Kansas City, Missouri; [e]The George Institute for Global Health, Sydney, New South Wales, Australia; [f]Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia; [g]Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine, Houston, Texas; [h]Division of Cardiology, UT Southwestern Medical Center, Dallas, Texas; [i]Baylor College of Medicine, Houston, Texas; [j]Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, Florida; [k]Emory Heart Disease Prevention Center, Emory University School of Medicine, Atlanta, Georgia; [l]Brigham and Women's Hospital Heart and Vascular Center, Harvard Medical School, Boston, Massachusetts; and the [m]Center for Preventive Cardiology, Knight Cardiovascular Institute, Oregon Health & Science University, Portland, Oregon. Dr. Shapiro has served on an Advisory Board for Esperion; has been a consultant to Amarin; and has received institutional grant/research support from the National Institutes of Health (NIH), Akcea Therapeutics, Amarin, and the FH Foundation. Dr. Morris has been a consultant to and served on an Advisory Board for Akcea Therapeutics; and has received research funding from Esperion. Dr. Kosiborod has been a consultant to and served on Advisory Boards for Amarin, Amgen, Applied Therapeutics, AstraZeneca, Bayer, Boehringer Ingelheim, Eisai, GlaxoSmithKline, Glytec, Eli Lilly, Intarcia, Janssen, Merck (Diabetes), Novartis, Novo Nordisk, and Sanofi; and has received research support from AstraZeneca, and Boehringer Ingelheim. Dr. Virani has received research grants from the Department of Veterans Affairs and World Heart Federation; and has received honoraria from the American College of Cardiology as associate editor for *Innovations*, acc.org. Dr. Ballantyne has been a consultant to Abbott Diagnostics, Akcea Therapeutics, Amarin, Amgen, Arrowhead, AstraZeneca, Boehringer Ingelheim, Denka Seiken, Esperion, Intercept, Janssen, Matinas BioPharma, Merck, Novartis, Novo Nordisk, Regeneron, Roche Diagnostic, and Sanofi-Synthelabo; and has received institutional grant/research support from Abbott Diagnostic, Akcea Therapeutics, Amgen, Esperion, Novartis, Regeneron, Roche Diagnostic, Sanofi-Synthelabo, NIH, American Heart Association, and the American Diabetes Association. Dr. Baum has served on Advisory Boards for Sanofi, Regeneron, Amgen, Novartis, and Akcea Therapeutics; has been a consultant to Sanofi, Amgen, Regeneron, Novo Nordisk, and Akcea Therapeutics; and has received speaker honoraria from Amgen, Boehringer Ingelheim, Nordisk, and Akcea Therapeutics. Dr. Bhatt has served on the Advisory Boards of Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, PhaseBio, and Regado Biosciences; has served on the Boards of Directors of the Boston VA Research Institute, the Society of Cardiovascular Patient Care, and TobeSoft; has served as Chair of the American Heart Association Quality Oversight Committee; has served on Data Monitoring Committees for the Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Cleveland Clinic (including for the ExCEED trial, funded by Edwards Lifesciences), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi-Sankyo), and Population Health Research Institute; has received honoraria from the American College of Cardiology (senior associate editor, *Clinical Trials and News*, ACC.org, and vice chair of the ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim), Belvoir Publications (Editor-in-Chief, *Harvard Heart Letter*), Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (Editor-in-Chief, *Journal of Invasive Cardiology*), *Journal of the American College of Cardiology* (guest editor; associate editor), Medtelligence/ReachMD (CME steering committees), Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national coleader, funded by Bayer), Slack Publications (chief medical editor, *Cardiology Today's Intervention*), Society of Cardiovascular Patient Care (secretary/treasurer), and WebMD

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ABSTRACT

Although significant progress has been made to reduce the global burden of cardiovascular disease, efforts have focused primarily on treatment of manifest disease rather than on prevention of events. An enormous opportunity exists to transition focus from intervention to providing equal attention to prevention of cardiovascular disease. The nascent specialty of "preventive cardiology" is emerging from the background of long-established services such as lipid, diabetes, hypertension, and general cardiology clinics. It is incumbent on the cardiology community to invest in cardiovascular prevention because past gains are threatened with the rising tide of obesity and diabetes. Now is the time to establish a dedicated preventive cardiology subspecialty to train the clinicians of the future. This American College of Cardiology Council Perspective aims to define the need for preventive cardiology as a unique subspecialty, broaches controversies, provides a structure for future training and education, and identifies possible paths forward to professional certification.
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Over the last 4 decades, we have witnessed significant reductions in morbidity and mortality from cardiovascular disease (CVD) (1). Nonetheless, CVD remains the leading killer in both men and women across the globe. What is less recognized, however, is that at least one-half of what has been achieved in terms of improvement in CVD outcomes relates to greater access to procedural interventions and technological advancements that allow patients to live and cope with advanced atherosclerotic cardiovascular disease (ASCVD) and heart failure rather than preventing the disease in the first place (2). Although avoiding earlier death, these individuals are at high risk for disability, and their continued clinical needs are associated with significant cost to the health care system. As declines in cardiovascular (CV) mortality are reaching a nadir, our health care system is unable to support additional therapies, particularly those that are prohibitively expensive and with modest impact on risk reduction. Furthermore, past gains are threatened by the expanding epidemics of obesity and diabetes (3), and this has brought to the forefront the practical value and need for expansion of structured and comprehensive interventions to prevent CVD. Indeed, it is likely that a paradigm shift is necessary to fulfill the promise of improving CV health in the population at large. Put another way, the real revolution in CVD prevention will occur when greater efforts and resources are applied to all preventive efforts (secondary, primary, and primordial prevention) (4). As such, preventive cardiology as a unique

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HIGHLIGHTS

- The medical community must invest in cardiovascular disease prevention because past gains are threatened by increased rates of obesity and diabetes.
- An enormous opportunity exists to transition focus from intervention to prevention of cardiovascular disease.
- Given the array of dedicated skills necessary to manage cardiovascular risk, the specialty of "preventive cardiology" is emerging.

subspecialty is emerging naturally and spontaneously as a separate discipline providing a comprehensive approach to a sector of CV care with enormously increasing demand. However, this subspecialty is in its infancy and remains fragmented and disorganized at all levels, from education and training, to implementation, operations, and coordination with standard of care services. This subspecialty will not realize its full potential until political barriers are transcended, training is standardized, structured, and delivered as part of dedicated fellowships, and recognition by a national certifying body is achieved (5). What follows is a critical examination of the need for the development of preventive cardiology as a subspecialty, highlighting the barriers to its maturation and the opportunities for successful implementation and growth.

A HISTORICAL PERSPECTIVE OF PREVENTIVE CARDIOLOGY—HOW WE GOT HERE

The Framingham Heart Study, launched in 1948, established the principle of CV risk, with its compounding predictive factors (6). Early work from Framingham opened up the whole field of preventive cardiology by identifying modifiable risk factors for heart disease. Next, clinical trials extended the epidemiological findings to demonstrate that managing hypercholesterolemia, hypertension, cigarette smoking, and diabetes reduced the risk for ASCVD across age and sex (7). Indeed, since the landmark publication of 4S study (Scandinavian Simvastatin Survival Study) in 1994, an uninterrupted stream of randomized controlled trials validated the effectiveness of statin drugs in virtually all clinically relevant patient groups (8). Due to the success of several early studies, trial design progressed from placebo-controlled to statin-controlled (high-intensity vs. low- or moderate-intensity) studies. The clinical outcomes from these studies suggested that there was no low-density lipoprotein cholesterol (LDL-C) level below which patients did not receive further benefit, thus setting the stage for the current standard of statin recommendation for all individuals above a certain risk threshold. The improved CVD outcomes observed across the statin mega-trials were impressive and strikingly consistent. Moreover, the results of these studies transformed the way clinicians perceived hypercholesterolemia and combined dyslipidemia, both in terms of risk assessment and treatment.

As the understanding that LDL-C lowering is safe, easy to achieve, and effective at mitigating atherosclerotic risk in broad populations became widely established, several national and international guidelines adopted LDL-C lowering as a top priority for ASCVD risk management. At the same time, proper risk assessment became a key driver of treatments that are long-term and occasionally associated

ABBREVIATIONS AND ACRONYMS

ABIM = American Board of Internal Medicine

ACC = American College of Cardiology

AHA = American Heart Association

ASCVD = atherosclerotic cardiovascular disease

CAC = coronary artery calcium

CV = cardiovascular

CVD = cardiovascular disease

EPA = eicosapentaenoic acid

FDA = U.S. Food and Drug Administration

IMT = intima-media thickness

LDL-C = low-density lipoprotein cholesterol

Lp(a) = lipoprotein(a)

MACE = major adverse cardiovascular events

MI = myocardial infarction

PCSK9 = proprotein convertase/subtilisin kexin type 9

TABLE 1 Components of an Academic Preventive Cardiology Program

Clinical staff	Specialized physicians	Advanced practice providers	Clinical pharmacist	Dietitian	Genetic counselor	Registered nurse
Services	Daily outpatient clinics	Counseling on diet, exercise, and smoking cessation	Cardiac rehabilitation	PCSK9 inhibitor clinic	LDL apheresis	Outreach clinics and telemedicine
Diagnostics	Lipid and biomarker laboratory	Subclinical atherosclerosis imaging (CIMT, CACS, CCTA)	Genetic testing	Ambulatory blood pressure monitoring	Echocardiography	Stress testing
Education	Preventive cardiology fellows	General cardiology fellows	Internal medicine residents	Medical students	Visiting physicians	Classes for patients, staff, and the public
Research	Basic science in lipids and vascular biology	Translational studies	Clinical research (family studies, cohorts, EMR)	Epidemiological studies	Clinical trials of novel therapeutics and devices	Registry and biorepository

CACS = coronary artery calcium score; CCTA = coronary computed tomography angiography; CIMT = carotid intima-media thickness; EMR = electronic medical record; LDL = low-density lipoprotein; PCSK9 = proprotein convertase/subtilisin kexin type 9.

with side effects. Specialty lipid clinics emerged to optimize implementation of evidence-based guidelines for lipid-lowering therapies, to provide management for patients with high-risk genetic lipid disorders, and for consultative guidance in the setting of treatment-associated adverse effects. However, it has become increasingly recognized that cholesterol management is most often required for individuals whose ASCVD risk is driven by a multiplicity of comorbidities and risk exposures. Thus, lipid management is 1 component of a comprehensive intervention addressing multiple important ASCVD risk factors, often including a combination of therapeutic lifestyle changes and medical therapies. This concept should be extended to the management of hypertension, diabetes, obesity, and suboptimal lifestyle habits, and so on—all of which can be addressed under the auspices of a dedicated preventive cardiology program. As the need to identify more comprehensive preventive opportunities in larger populations emerged, the value of the limited specialty clinic model diminished and the roots of preventive cardiology took hold. It became increasingly apparent that to prevent ASCVD most effectively, multiple risk factor interventions are required.

Global risk assessment tools have limitations, with prior algorithms underestimating and more modern risk scores at times overestimating risk. Moreover, risk assessment tools for ASCVD, although helpful, continue to exhibit gaps, such as not accounting for the risk of heart failure, and also require frequent updating to incorporate contemporary data (9). Current work moves from population-level data and risk factors, such as cholesterol, to a new generation of precision medicine and tailored therapeutics. Within the realm of preventive cardiology, refinement in risk estimation and therapeutic decision making is being facilitated by atherosclerosis imaging (e.g., ultrasound for carotid intima-media thickness and carotid plaque, computed tomography for coronary artery calcium score), new biomarkers, advances in genetic testing (identification of causal monogenic mutations and development of actionable polygenic risk scores), and a plethora of pipeline and market pharmaceuticals with promise or proof of benefits. Given the proliferation of new data, approaches, and pharmacotherapy, preventive cardiology needs a structure to deliver specialized training and produce dedicated clinician-scientists and practitioners to serve this ever-growing medical need (**Table 1**). This new direction will be important to help us define risks early, initiate appropriate treatments, and identify new drugs/approaches for treatment and prevention. **Table 2** delineates common indications for referral to preventive cardiology services.

TABLE 2 Common Indications for Referral to Preventive Cardiology Services

Cardiovascular risk assessment
Nutritional interventions
Lifestyle counseling
Smoking cessation
Cardiac rehabilitation
Family history of premature ASCVD
Personal history of ASCVD, particularly in individuals <60 yrs of age
Inherited and/or severe dyslipidemias
Evaluation and management of SAMS
LDL apheresis
Genetic testing
Noninvasive atherosclerosis imaging
Optimization of hypertension management
Optimization of diabetes management
Participation in clinical trials

ASCVD = atherosclerotic cardiovascular disease; LDL = low-density lipoprotein; SAMS = statin associated muscle symptoms.

LIPID-RELATED RISK. Scientists and clinicians from varied backgrounds have been drawn to the relation between cholesterol and ASCVD since 1913 when Nikolai Ansitschkow, a Russian pathologist, fed pure cholesterol to rabbits to induce aortic atherosclerosis (10). The Framingham Heart Study launched the concept of risk factors for ASCVD, a model that is just as important today (6). Years later, John Gofman, a physicist, defined plasma lipoproteins using analytical ultracentrifugation, and demonstrated the direct and inverse relationships LDL-C and high-density lipoprotein cholesterol levels, respectively, have with rates of myocardial infarction (11). Ten years later, Konrad Bloch and Feodor Lynen were awarded the Nobel Prize for determining the complex metabolic pathway of cholesterol synthesis (12). In 1973, Michael Brown and Joe Goldstein made their groundbreaking discoveries related to the LDL receptor, with the original inspiration for their work being a young child who sustained a heart attack due to homozygous familial hypercholesterolemia (13,14).

The Lipid Research Clinics-Coronary Primary Prevention Trial with cholestyramine and the Coronary Drug Project with niacin ushered in the era of lipid modulation for prevention of heart disease (15–17). These studies gave birth to the concepts of primary and secondary prevention of CVD and paved the way for the development and utilization of the statin drugs, an incredible journey since lovastatin entered the market in 1987 (18).

Mere decades ago, atherosclerosis was seen as an inevitable consequence of aging—a degenerative disease about which nothing could be done. Today, prevention of ASCVD has acquired status as an effective, practical, and widely applicable art. The disease is eminently preventable, and lowering blood cholesterol is always effective, though often marginally, irrespective of the original drivers of the disease.

EMERGING SCIENCE IN CVD RISK REDUCTION. The relatively recent discovery of proprotein convertase/subtilisin kexin type 9 (PCSK9) as a master regulator of plasma LDL-C has revolutionized our understanding of lipid metabolism (19,20). Two fully human monoclonal antibodies that antagonize PCSK9 action were approved by the U.S. Food and Drug Administration (FDA) just 12 years after the discovery of this protein, and landmark trials have demonstrated incremental improvement in CV outcomes when these agents are combined with statins (21,22). Alternative strategies to inhibit PCSK9 are in advanced development (23).

Beyond LDL-C, enthusiasm and momentum are building around targeting other atherogenic lipoproteins. Both observational and genetic epidemiology suggest that triglycerides and lipoprotein(a) [Lp(a)] levels are likely to become targets of therapy to further improve CV outcomes. Randomized controlled studies are assessing CV outcomes by targeting triglycerides with omega-3 polyunsaturated fatty acids (eicosapentaenoic acid [EPA] only or a combination of EPA and docosohexaenoic acid) and a novel selective peroxisome proliferator-activated receptor alpha modulator, pemafibrate (24–26). In fact, the recently reported REDUCE-IT (Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial), testing the addition of 4 g/day of EPA on top of statin therapy versus placebo in patients with established ASCVD and/or diabetes, and at least 1 additional risk factor, demonstrated remarkable improvements in CV outcomes (27). Volanesorsen, an antisense oligonucleotide that blocks production of apoC III, has demonstrated profound triglyceride-lowering capability and apparent safety (28). The second-generation (*N*-acetylgalactosamine version) of this drug, Akcea, ApoCIII-Lrx, is currently being evaluated in a Phase IIB clinical trial. Moreover, Lp(a) has taken on considerable importance with the development of a specific antisense oligonucleotide that inhibits apolipoprotein(a) production and thus dramatically lowers plasma Lp(a) concentrations by approximately 80% (29,30). A large, randomized controlled trial testing whether Lp(a) reduction is associated with improved CV outcomes is being designed. As delineated in the preceding text, lipid science and translation to patient management have and continue to evolve, requiring subspecialty knowledge to optimize evaluation and management of patients at risk for CVD events. The basic role of the primary care provider in managing CV risk should be and likely will continue unchanged, even after specialized preventive cardiology services are available in all major markets. However, select patients will benefit from evaluation and management from a dedicated preventive cardiology service for accurate CVD risk assessment and optimal management inclusive of lifestyle, supplemental, and pharmacological therapy.

INFLAMMATORY RISK. ASCVD event rates are unacceptably high, even among patients intensively treated with existing therapies. The concept of residual CV risk implies that outcomes may be improved by targeting other CV risk factors and comorbidities after LDL-C is lowered maximally. As an example, in the FOURIER (Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk) trial of evolocumab (a PCSK9 inhibitor), there was a modest absolute risk reduction (1.5%) of the primary composite major adverse CV outcome despite achieving a median LDL-C of 30 mg/dl (21). Thus, there has been great interest in exploring other avenues to optimize CV outcomes.

The inflammatory hypothesis of atherosclerosis was tested clinically in the CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcomes Study), which enrolled 10,061 subjects with established ASCVD and evidence of subclinical inflammation (based on elevated high-sensitivity C-reactive protein levels) and randomized to optimal medical therapy plus either the interleukin-1β antagonist canakinumab or placebo. A statistically significant reduction in risk of recurrent events was seen among those allocated to canakinumab (31). Thus, inflammation can be added to the list of drivers of residual risk. To that end, a number of additional anti-inflammatory agents are currently being tested or evaluated for reduction of ASCVD events. The road ahead for regulatory approval and clinical implementation of potent anti-inflammatory agents for secondary prevention is likely to be twisted and arduous. In fact, Novartis officially withdrew its application to the Committee for Medicinal Products for Human Use of the European Medicines Agency for a marketing authorization of canakinumab for secondary prevention.

The CIRT (Cardiovascular Inflammation Reduction Trial), testing low-dose methotrexate versus placebo in high-risk patients, failed to demonstrate an

improvement in CV outcomes, suggesting that targeting specific inflammatory pathways will be necessary to garner therapeutic benefits (32). Indeed, there are ongoing studies testing the inflammatory hypothesis of ASCVD by suppressing inflammation with alternative approaches, including trials evaluating the role of low-dose colchicine for secondary prevention of CVD (33,34). The preventive cardiologist of the future will need to be well versed in assessing inflammatory risk and potentially modulating this risk with specific anti-inflammatory therapies.

DIABETES THERAPIES—FROM GLUCOSE CONTROL TO CV RISK MANAGEMENT. Type 2 diabetes confers a high lifetime risk for developing CVD (35). This association is further compounded by the fact that other metabolic risk factors for both ASCVD and heart failure (HF) are commonly found in patients with diabetes. Indeed, the major medical threats among those with diabetes are ASCVD and heart failure (both with reduced, and increasingly with preserved, left ventricular ejection fraction, which can develop even in the absence of clinically manifest ASCVD) (36). Although the role of glycemic control in prevention of certain microvascular complications is clear, targeting plasma glucose as a strategy to mitigate ASCVD and HF risks has failed to demonstrate significant benefit.

In the UKPDS (United Kingdom Prospective Diabetes Study) of 5,102 individuals with newly diagnosed diabetes, intensive glycemic control did not improve CV outcomes as compared with the standard control arm (glycosylated hemoglobin <9%) (37). Additionally, meta-analyses of the UKPDS, ACCORD (Action to Control Cardiovascular Risk in Diabetes) study, ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) trial, and VADT (Veteran Affairs Diabetes Trial) demonstrated that intensive therapy, compared with conventional therapy, is associated with adverse events, namely hypoglycemia, without a significant reduction in CV events (with no effects on CV death or hospitalization for heart failure), despite a reduction in microvascular complications (38). Furthermore, as newer diabetes agents were developed, concerns for possible CV harm associated with certain classes of glucose-lowering medications came to the fore, leading to the FDA mandate for dedicated large CV outcomes trials to demonstrate CV safety, as part of the drug approval process (39). In that regard, for years, the medical community celebrated the arrival of antidiabetic agents with no impact on CV outcomes.

Now, a revolution is underway since the arrival of new antidiabetic drugs that demonstrate improved CV outcomes. The landmark EMPA-REG OUTCOME trial (BI 10773 [Empagliflozin] Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients) compared empagliflozin (an SGLT-2 inhibitor) to standard care in 7,020 high-risk diabetes patients with established CVD and reported a 14% reduction in the composite outcome of major adverse cardiovascular events (MACE [myocardial infarction (MI), stroke, and CV death]), and a 35% reduction in heart failure hospitalizations over 3 years of follow-up (40). Subsequent analyses indicated that these CV benefits of empagliflozin appear to be independent of its glucose-lowering effects (41). The FDA has included reduction of risk of CV death in patients with diabetes and established ASCVD as an indication for empagliflozin—a first CV indication for a type 2 diabetes agent in history. Some of these findings were replicated in the CANVAS (Canagliflozin Cardiovascular Assessment Study), in which another SGLT-2 inhibitor, canagliflozin, reduced MACE by 14% during a median follow-up of 3.6 years in 10,142 patients with diabetes (ultimately leading to approval of canagliflozin by the FDA for reducing the risk of MACE in patients with type 2 diabetes and ASCVD), with similar reductions in hospitalizations for HF (42). Finally, in the DECLARE (Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events)—the largest SGLT-2 inhibitor CV outcomes trial to date, which incorporated the majority of type 2 diabetes patients without known ASCVD—demonstrated a significant reduction in the composite of CV death and heart failure hospitalizations, even within the subgroup of lower-risk patients, extending the benefits of SGLT-2 inhibitor class to the primary prevention patient population (43). Furthermore, all 3 trials demonstrated a marked reduction in the progression of kidney disease—another feared and morbid complication of type 2 diabetes, with significant health care cost implications.

The GLP-1 receptor agonists liraglutide and semaglutide have also demonstrated CV benefits in individuals with diabetes and higher risk for CVD. In the LEADER (Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcomes Results—A Long Term Evaluation) trial, 9,340 patients with diabetes at high risk for CVD or with known CVD were followed over 3.8 years (44). A 13% reduction in risk for the primary outcomes of stroke, MI, or CV death was observed in patients receiving liraglutide compared with placebo, and an independent significant reduction in CV death. The FDA has subsequently approved the use of liraglutide for reducing

the risk of MACE in individuals with type 2 diabetes and known CVD. Since then, more evidence continues to emerge regarding the ASCVD benefits of GLP-1 receptor agonists, including the data from the HARMONY OUTCOMES (Effect of Albiglutide, When Added to Standard Blood Glucose Lowering Therapies, on Major Cardiovascular Events in Subjects With Type 2 Diabetes Mellitus) trial, which demonstrated a robust 22% relative risk reduction in MACE with albiglutide, another long-acting GLP-1 receptor agonist, as compared with placebo, and a 25% risk reduction in recurrent MI among patients with type 2 diabetes and established ASCVD (45). The improved outcomes were observed despite the modest metabolic effects of albiglutide (including glycosylated hemoglobin and weight loss effects), suggesting once again that the mechanisms of these beneficial effects are likely unrelated to their glucose-lowering properties.

The positive results of all of these CV outcomes trials have galvanized the cardiology community and should expand the boundaries of preventive cardiology well beyond lipid management. However, cardiologists currently prescribe only approximately 5% of all SGLT-2 inhibitors, with the lion's share of these effective drugs being prescribed by primary care providers and endocrinologists. Moreover, these trends did not change 1 year after the FDA broadened the labeling of empagliflozin (46). The American College of Cardiology (ACC) is actively addressing these treatment gaps in a number of ways, including the recent publication of the "2018 ACC Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease" (47). Indeed, optimal management of patients with diabetes is quickly becoming one of the most important facets of preventive cardiology, and dedicated practitioners will need to be facile with newer (and developing) therapies demonstrated to improve CV outcomes in this high-risk group.

THE THREAT OF OBESITY. Along with type 2 diabetes, the risk factor whose incidence has moved in the wrong direction is obesity. In fact, the obesity epidemic threatens to blunt the CV gains that have accrued over the last 50 years. Comprehensive lifestyle intervention remains the foundation for weight loss and the initial step in the management of obesity according to the ACC/American Heart Association (AHA) guidelines (48). Pharmacotherapy and bariatric surgery are important adjuncts for the management of obesity when lifestyle modification is inadequate. Numerous antiobesity drugs have been available over the years, however, there have been significant CV safety concerns (49). Currently, there are 5 antiobesity drugs that are FDA approved, including orlistat, lorcaserin, naltrexone-bupropion, phentermine-topiramate, and liraglutide (50). Practicing clinicians, including preventive cardiologists, must be knowledgeable and facile with these agents and be able to discuss the potential risks and benefits of these therapies with patients (50). Although these drugs can be used as adjuncts to lifestyle therapy, they remain expensive, and there is a high risk of regaining weight following discontinuation.

For patients who do not achieve targeted weight loss goals with lifestyle modification and/or pharmacotherapy, bariatric surgery is an option. Bariatric surgery induces sustained weight loss and leads to improvement in obesity related comorbidities such as diabetes (50). The STAMPEDE (Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently) trial evaluated the efficacy of bariatric surgery compared with intensive medical therapy in patients with type 2 diabetes (51). Patients who underwent bariatric surgery were more likely to achieve weight loss, glycemic targets, and better quality-of-life measures compared with those in the intensive medical therapy-only group (51,52). Importantly, these findings were sustained at 5-year follow-up (53). The evidence demonstrates that metabolic surgery is the most effective means of attaining significant and long-lasting weight loss in obese individuals (50). These randomized trials also demonstrate the superiority of surgery over medical treatment alone in achieving euglycemia and improvement in other traditional CV risk factors (53,54). Moreover, observational studies suggest that the noted reduction in risk factors translates to a reduction in major adverse CV events and CV mortality (55–57). The preventive cardiologist must become acquainted with these advances in the medical and surgical management of obesity. Furthermore, we contend that the logical home for obesity management is within future centers for preventive cardiology. As such, prospective preventive cardiology practitioners must become adept at the evaluation and medical management of individuals with obesity.

HYPERTENSION. Hypertension is a well-established, independent causal risk factor for CVD and treatment of high blood pressure reduces morbidity and mortality (58). Despite the availability of numerous effective pharmacological treatment options, high blood pressure continues to be a significant cause of morbidity and mortality, with the number of deaths

attributed to it increasing by 37.5% from 2005 to 2015 in the United States (59). The 2017 ACC/AHA guidelines for the prevention, detection, evaluation, and management of high blood pressure established a new definition of hypertension as systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥80 mm Hg (58). This new guideline recommendation was largely based on evidence provided by the SPRINT trial (Systolic Blood Pressure Intervention Trial) (60,61). On the basis of this new definition, it is estimated that the overall prevalence of hypertension among U.S. adults is 45.6% according to a study based on data from the National Health and Nutrition Examination Survey (62). More importantly, <50% of patients taking antihypertensive medications meet current blood pressure goals, representing another important area of focus for the prevention of CVD (62).

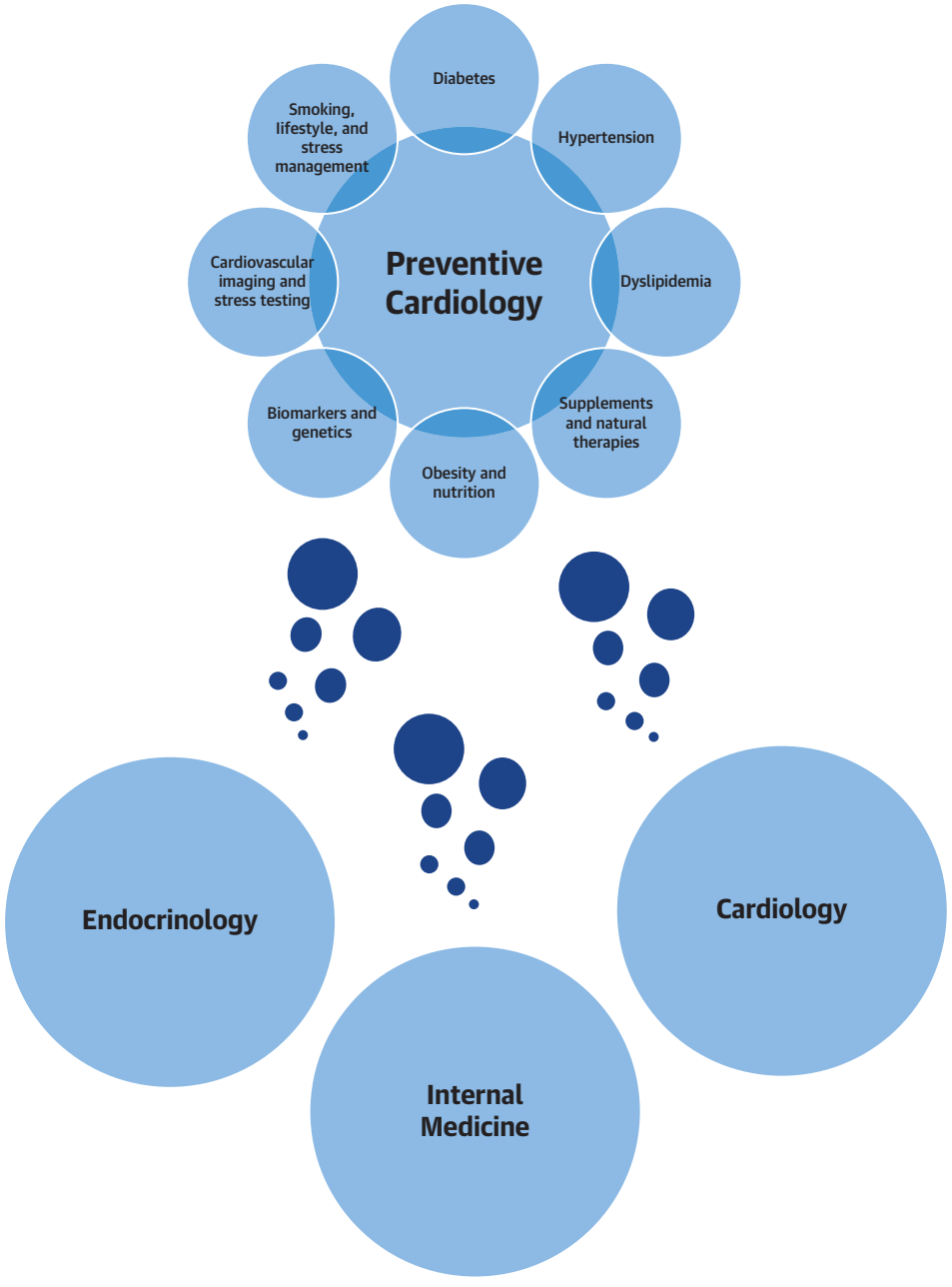
A number of new pharmacological and nonpharmacological therapies are currently under development for the management of hypertension. Several novel drug classes under investigation include vasopeptidase inhibitors, aldosterone synthase and soluble epoxide hydrolase inhibitors, natriuretic peptide A agonists, and vasoactive intestinal peptide receptor 2 agonists (63,64). Vaccines against angiotensin II and its receptor type 1 are in preclinical stages (64). There has been excitement over novel catheter-based interventions such as renal denervation and baroreflex activation therapy that may be promising as adjuncts to conventional treatment options (65). Given the epidemic of hypertension and its close association with the development of ASCVD, preventive cardiologists should play a key role in the management of high blood pressure and mitigating the associated morbidity and mortality.

ANTIPLATELET AND ANTITHROMBOTIC THERAPY. Aspirin for primary prevention of ASCVD has recently been tested in 3 large randomized placebo-controlled trials. There was no significant reduction in the risk of CV events in patients at moderate risk (66). Cardiovascular events were reduced modestly in patients with diabetes, but this benefit was in part counterbalanced by an increase in major bleeding events (67). Among older adults, low-dose aspirin for primary prevention resulted in a significantly higher risk of major bleeding but did not lower risk of CV events as compared with placebo (68). As a result of these trials, evidence does not support the universal use of aspirin for primary prevention except in those at high risk of ASCVD without increased bleeding risk (69,70). A more targeted aspirin use after a discussion between the patient and preventive cardiologist might be considered in high-risk patients. Again, this is an area where specific understanding of the nuances of the data, use of risk calculators, and the skill set of the preventive cardiologist would be particularly useful.

Low-dose aspirin for secondary prevention remains a class IA recommendation for people with ASCVD, and treatment with clopidogrel is reasonable when aspirin is contraindicated (71). The ADAPTABLE trial is being conducted to compare low-dose (81 mg) with high-dose (325 mg) aspirin to establish which dosage of aspirin is best for secondary prevention of ASCVD (72). Dual antiplatelet therapy (aspirin plus a $P2Y_{12}$ inhibitor) is recommended for 12 months in patients with a history of acute coronary syndrome. The optimal duration beyond 12 months is uncertain (73). Recently, it was announced that the Phase III THEMIS study (Effect of Ticagrelor on Health Outcomes in Diabetes Mellitus Patients Intervention Study) trial met its primary endpoint and demonstrated that ticagrelor, taken in conjunction with aspirin, demonstrated reduction in a composite of MACE compared with aspirin alone in over 19,000 patients with coronary artery disease and type 2 diabetes with no prior heart attack or stroke (74). Moreover, the COMPASS (Cardiovascular Outcomes for People Using Anticoagulation Strategies) trial tested the hypothesis that a low dose of the direct-acting anticoagulant rivaroxaban in combination with aspirin or given alone is more effective than aspirin alone for secondary prevention of CV events in patients with ASCVD (75). Those randomized to rivaroxaban (2.5 mg twice daily) plus aspirin had better CV outcomes but more major bleeding events than those assigned to aspirin alone. Rivaroxaban alone (5 mg twice daily) did not result in better CV outcomes than aspirin alone and caused more major bleeding events. The discussion around potentially initiating antithrombotic therapy is a prime example where the preventive cardiologist will be uniquely suited to individualize the risk-benefit ratio and facilitate shared decision making.

TOBACCO CESSATION TREATMENT. Tobacco use remains the leading preventable cause of morbidity and mortality worldwide (76). Although there has been a significant decline in tobacco abuse over the last several decades, the prevalence of smoking among U.S. adults remains unacceptably high. Almost one-third of the deaths in the United States related to cigarette smoking are secondary to CVD (76). Moreover, smoking unfavorably affects all stages of atherothrombosis, including endothelial dysfunction (77), initiation, progression, and destabilization of atherosclerotic plaque (78) and favors a

CENTRAL ILLUSTRATION **The Necessary Competencies for Preventive Cardiology**



Shapiro, M.D. et al. J Am Coll Cardiol. 2019;74(15):1926–42.

The set of competencies for preventive cardiology encompasses aspects of care traditionally within the realm of established disciplines such as internal medicine, endocrinology, and cardiology. The preventive cardiologist of the future will be equally proficient in metabolic management and cardiovascular disease management through expert use of diagnostic and therapeutic interventions inclusive of nonpharmacological tools (i.e., natural therapies, diet, and behavior modification strategies).

prothrombotic state (79,80). As such, smoking increases the risk of ASCVD events (81-83). Additionally, tobacco use is associated with an increased risk of heart failure (84), and coronary artery disease subjects who continue to smoke after revascularization are at increased risk of stent thrombosis (85).

Smoking cessation reduces the risk of CVD events by as much as 50%, an intervention associated with

TABLE 3 Components of a Preventive Cardiology Fellowship

Primary and secondary prevention clinics	Cardiovascular risk assessment, genetic and complex lipid disorder management, obesity, smoking cessation, combination lipid therapies, antithrombotic strategies, natural therapies, women's cardiovascular health, lifestyle counseling, genetic testing
Diabetes clinic	Optimal management of type 2 diabetes and metabolic syndrome, in cooperation with diabetes center when appropriate
Hypertension clinic	Optimal management of hypertension, in cooperation with hypertension clinic when appropriate
Cardiac imaging	Coronary artery calcium score, coronary CTA, CIMT, abdominal aortic ultrasound, echocardiography, and stress testing methodologies
Cardiac rehabilitation	Core components and delivery of phase 2 cardiac rehabilitation services
LDL apheresis	Exposure to/knowledge of LDL apheresis
Research	Basic, clinical, translational, or health services research in preventive cardiology

Abbreviations as in Table 1.

much greater risk reduction than any other available therapy (86,87). The benefits of smoking cessation apply to all subgroups, including those who quit after the development of clinical CVD. Evidence demonstrates that tobacco cessation programs are cost-effective and compare favorably with the management of other CVD risk factors (88,89). Both behavioral interventions and medications, especially when provided together, are associated with benefit. A recent ACC statement has reminded us of the steps to be taken for effective risk reduction interventions in practice (90).

The scope of preventive cardiology services should include the provision of behavioral and pharmacological interventions for tobacco users. It must be kept in mind that interventions exclusively directed at smoking cessation are either not reimbursed or reimbursed at levels that are too low for a sustainable service. Therefore, it is incumbent on the preventive cardiologist to acquire the skill set to address this problem competently and effectively in the context of risk management.

SUBCLINICAL ATHEROSCLEROSIS IMAGING. Risk estimation is the starting point for therapeutic decision making for the primary prevention of ASCVD (91). However, as mentioned earlier, global risk assessment scores have limitations with regard to accurate risk prediction. Noninvasive imaging for subclinical atherosclerosis can be used in conjunction with global risk scores to refine individual risk estimation if there is clinical uncertainty and, more importantly, to facilitate shared decision making (91). In particular, the coronary artery calcium (CAC) score has accrued the most robust data to support its clinical utility in detecting subclinical atherosclerosis and refining risk assessment (92). Over the past 3 decades, computed tomography for CAC scoring has emerged as a safe, noninvasive modality for identifying the presence or absence of coronary atherosclerosis. Although the presence and severity of atherosclerosis is a strong predictor of future CV events (93), the absence of CAC is associated with an extremely low event rate, even in those who have multiple risk factors (94–97) or those who meet current criteria for statin therapy (98,99). Furthermore, data from several studies suggest that the identification of CAC promotes more aggressive pharmacological and lifestyle therapies (100). Moreover, among individuals who have coronary atherosclerosis detected by computed tomography, statin therapy has been shown to be associated with a significant reduction in CV events (101–103). However, as atherosclerosis is a systemic disease involving multiple vascular beds including large and medium sized vessels such as the carotid, aorta, coronary and peripheral arteries, imaging studies of multiple vascular territories may provide a more complete overview of the burden of atherosclerosis (104). From a practical standpoint, ultrasound-based imaging of the carotid arteries for measurement of intima-media thickness (IMT) and plaque has also emerged as a reasonable noninvasive modality for enhancing risk assessment.

Recently, a group of investigators performed carotid intima-media measurement in over 3,000 subjects and found that sharing scans showing the extent of atherosclerosis to patients and their doctors resulted in a decreased risk of CVD 1 year later, compared with the use of standard information regarding CVD risk (105). Noninvasive atherosclerosis imaging has the ability to provide insight into the lifetime exposure to both known and unknown risk factors, as well as the mostly unknown resilience factors that reduce vulnerability to atherosclerosis. Expertise in subclinical atherosclerosis imaging is likely to be one of the most critical skills that will fall within the domain of preventive cardiologists, especially given recent changes in the AHA/ACC cholesterol guidelines and secular changes in out-of-pocket cost (and perhaps future reimbursement) for testing.

PROPOSAL FOR PREVENTIVE CARDIOLOGY AS A SUBSPECIALTY OF CARDIOVASCULAR MEDICINE

Preventive cardiology is in a critical growth spurt that will define its future structure and scope. Historically, the field has contributed much understanding to the epidemiology of ASCVD, defining traditional risk factors, and informing public health policy. Currently, it is embracing new preventive therapies and targets associated with greater risk reduction at the primary and primordial level. Moreover, advances in risk assessment, including novel biomarkers, genetics, and noninvasive subclinical atherosclerosis imaging represent major advances that are likely to be applied more widely in the near future. Issues related to primary and secondary prevention are becoming increasing complex, and more and more patients are seeking specialized advice on CVD risk assessment and management. Given the increasing intricacies in evaluating and managing CVD risk, there is a mandate for the formation of a new subspecialty of CV medicine (**Central Illustration**).

Since the first discussions of preventive cardiology as a dedicated subspecialty, there have been multiple perspectives as to which clinicians are best suited and qualified to take on this role. The preventive cardiologist of the future will need to have specialty knowledge of CV physiology and imaging, coronary anatomy, electrocardiography, and stress testing, and thus this subspecialty naturally falls within the purview and skillset of CV medicine. Subspecialty training for preventive cardiology should be an option for advanced training after general cardiology fellowship training, just as is required for advanced heart failure management, congenital heart disease, interventional cardiology, and electrophysiology. However, as contrasted to other subspecialties of CV medicine, the preventive cardiology fellowship should be made available to other specialists, such as internists, endocrinologists, family physicians, and other board-certified providers, according to pre-specified qualification requirements. It is nonetheless evident that cardiology fellowship training provides the didactic and practical knowledge of CVD and its consequences, far more so than any other specialty. A cardiologist's familiarity with this disease stems from structured theoretical education, patient care, training in CV imaging, and exposure to cardiac catheterization laboratory procedures and to cardiac rehabilitation services. Cardiology fellows are immersed in risk evaluation and implications for clinical management from the beginning of training. From a practical standpoint, a preventive cardiologist with general cardiology training will have the ability to manage all facets of primary and secondary prevention. Advanced training in lipid metabolism and management, hypertension, type 2 diabetes, platelets and anticoagulation, obesity, nutrition, supplemental therapies, and atherosclerosis imaging should all be provided in the preventive cardiology fellowship. Although this vision may be seen as partisan and dogmatic, we need to clarify that our concept of preventive cardiology as a subspecialty of cardiology in no way limits other clinicians from practicing the prevention of CVD according to the current standards of care and training. Rather, we propose that the designation of a board-certified preventive cardiologist belongs in the domain and infrastructure of cardiovascular medicine. We envision a convergence of these 2 positions, with the preventive cardiology fellowship being open to other applicants, as described in the preceding text. Of course, for preventive cardiology to become a mature discipline, worthy of subspecialty status, numerous gaps need to be filled.

As the leading organization for CV professionals in the United States, the ACC needs to play a key role in the development and provision of the subspecialty of preventive cardiology. Many other professional societies, such as the AHA, American Society for Preventive Cardiology, the National Lipid Association, the Endocrine Society, and the American Diabetes Association, are also key stakeholders. However, the ACC has the potential to consolidate efforts around this growing discipline and take ownership of the entire subspecialty to provide a home for practitioners, set standards and practice guidelines, establish a certifying body and board certification process, and work toward implementation of preventive cardiology fellowship training programs.

FELLOWSHIP TRAINING

The cardiology community is undergoing a resurgence in CVD prevention due to a number of factors, including secular changes in CV risk factors, new understandings in CVD epidemiology, results from large CV outcomes trials, advances in drug development, and a move from the fee-for service-model toward value-based care. Despite the fact that improvement in lifestyle and implementation of preventive therapies are associated with improvement in clinical outcomes, these interventions are vastly underutilized. There are myriad underpinnings to this observation, though at least a substantial part

of this problem is likely due to the insufficient attention to education in CVD prevention during residency and fellowship training. Although there are a few preventive cardiology training programs around the country, they differ markedly in emphasis and approach (106), and are largely focused on providing specialized research experience to fellows, residents, and young scientists. Moreover, current competency standards in preventive cardiology for cardiology fellows are virtually nonexistent with a minimal exposure (1 month of dedicated training) requirement as set forth by the ACC 2015 Core Cardiovascular Training Statement (COCATS 4) Task Force 2: Training in Preventive Cardiovascular Medicine (107). Specifically, to meet this requirement, the task force recommended participation in a rotation devoted to preventive cardiology with exposure to cardiac rehabilitation, as well as diabetes, hypertension, and lipid clinics.

The aim of this document is to provide a rationale for the development of preventive cardiology as a new subspecialty of cardiovascular medicine, not to lay out a detailed list of training standards. Nonetheless, we conceive of this subspecialty fellowship as a dedicated 1- or 2-year training program that follows completion of an accredited general cardiology fellowship (**Table 3**). Entry in the subspecialty fellowship could also be granted to other qualified applicants, such as those who have completed a fellowship in endocrinology or simply residency in internal medicine but with additional accredited study in cardiometabolic disease management (such as diplomates from the American Board of Clinical Lipidology, or certified specialists in clinical hypertension). The purpose of this subspecialty fellowship is to prepare the budding preventive cardiologist with all of the theoretical and practical knowledge necessary to be an expert in the evaluation and management of patients with or at risk for ASCVD. The 1-year fellowship is purely clinical and suited for the trainee preparing for a career dedicated to patient care. The 2-year fellowship will include a robust research component (e.g., clinical, basic science, translational, or health outcome studies) that will prepare the trainee for an academic career that includes clinical responsibilities and research capabilities.

Preventive cardiology training programs will require appropriate faculty in terms of number and breadth of expertise to teach and mentor fellows. Faculty expertise should include atherosclerosis, lipoprotein metabolism, vascular biology, hypertension, diabetes, thrombosis, noninvasive atherosclerosis imaging techniques, genetics, exercise physiology, cardiac rehabilitation, nutrition, weight management, smoking cessation, CV epidemiology, natural therapies, and clinical pharmacology. Training programs should include exposure to cardiac rehabilitation classes, registered dietitians, clinical pharmacists, lifestyle counselors, and smoking cessation programs.

As in any training program, didactic instruction is an essential component for trainees. Didactics would include lectures, one-on-one sessions, conferences, journal clubs, grand rounds, and clinical case presentations. Clinical training would include experience in assessment of CV risk, management of complex dyslipidemia, hypertension, cardiometabolic risk, obesity medicine, novel risk factors, cardiac rehabilitation, atherosclerosis imaging, and implementation of all facets of lifestyle counseling (e.g., dietary interventions, weight management, exercise, smoking cessation, stress reduction, sleep hygiene, and so on). Preventive cardiology training must include exposure across all risk strata amongst individuals of all ages, sex, and ethnicity. Trainees should be exposed to patients with a history of revascularization, cardiac transplantation, and other complex CV procedures.

RECOGNITION AND CERTIFICATION

The culmination of subspecialty training is not only successful completion of an approved training program, but also recognition of competence as determined by a governing board or societal examination. This issue of subspecialty certification is of utmost importance and cannot be overstated. Preventive cardiology will not truly be an authentic subspecialty of CV medicine until it achieves these milestones. There are a number of certifying boards that oversee and administer nonaccredited specialties, but they fail to encompass the wider knowledge spectrum that should be required for a clinician to call oneself a preventive cardiologist. There are various options for recognition and subspecialty certification of preventive cardiology. Traditionally, the American Board of Internal Medicine (ABIM) has been the accrediting and certifying body for proposed specialties and subspecialties of internal medicine. They have set forth guidelines for creating new subspecialties that were published initially in 1993 and revised in 2006. The most recent document “New and Emerging Disciplines in Internal Medicine-2 (NEDIM-2)” delineates the standards for consideration of a new request (108). The major principle that underlies these recommendations is evidence that the proposed subspecialty is definable in terms of body of knowledge that is nonredundant with the parent

specialty, that a significant number of clinical training programs already exist, and that the unique clinical offerings of the discipline would enhance patient care. The ABIM applies these guidelines rigorously to all applications. Indeed, subspecialty applications from clinical pharmacology, vascular medicine, addiction medicine, and obesity medicine have not been approved to date as they did not meet 1 or more of these criteria or they were deemed insufficiently mature, as reflected by the number of training programs or practitioners in the field. In addition, the aforementioned American Board of Clinical Lipidology is not affiliated with the ABIM.

We propose another option for consideration—an ACC certification of clinicians who are able to demonstrate proof of training (preventive cardiology fellowship) and competence (certifying examination) in preventive cardiology (**Central Illustration**). We view this option as being preferable to pursuing jurisdiction under the ABIM. In this scenario, the ACC would set the standards for fellowship training, accredit training programs, and administer a certifying examination. The ACC has the expertise, leadership, primary interest, and experience to accomplish this goal. Nevertheless, the ACC would develop this model with input from partner organizations (e.g., American Society for Preventive Cardiology, American Diabetes Association, National Lipid Association, American Association of Cardiovascular and Pulmonary rehabilitation, etc.). These collaborations would ensure that training and certification are comprehensive and high value. The ACC would work with a preventive cardiology fellowship program task force to establish a core curriculum to train and certify cardiologists and other qualified participants, with the understanding that parallel programs may also develop to train qualified specialists in this area. Indeed, there are a variety of other excellent proposals for training, including 1 for the cardiometabolic specialist that represents a hybrid between cardiology and endocrinology training (109,110).

CONCLUSIONS

We are in the midst of a revolution in the prevention and management of CVD, with the emergence of new drugs and new targets associated with improved CV outcomes. At the same time, advances in risk assessment, including novel biomarkers, genetics, and noninvasive subclinical atherosclerosis imaging represent major advances that will be implemented more widely in the coming years. Issues related to primary and secondary prevention are becoming increasing complex, and more and more patients are seeking specialized advice on CVD risk assessment and management. There is a need for the formation of a new subspecialty of CV medicine. With advances in basic science, epidemiology, genetics, clinical trials, therapeutics, risk assessment, and CV imaging, the preventive CV specialist of the future will require training and expertise beyond what is currently delivered in standard fellowship training programs. We propose that the culmination and validation of these efforts should be the formation of a standardized fellowship program and certification exam, endorsed by the ACC.

ADDRESS FOR CORRESPONDENCE: Dr. Michael D. Shapiro, Center for Preventive Cardiology, Wake Forest University Baptist Medical Center, Medical Center Boulevard, Winston-Salem, North Carolina 27106. E-mail: mdshapir@wakehealth.edu. Twitter: @DrMichaelShapir.

REFERENCES

1. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. Circulation 2017;135:e146–603.

2. 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;356:2388–98.

3. Hossain P, Kawar B, El Nahas M. Obesity and diabetes in the developing world–a growing challenge. N Engl J Med 2007;356:213–5.

4. Vaduganathan M, Venkataramani AS, Bhatt DL. Moving toward global primordial prevention in cardiovascular disease: the heart of the matter. J Am Coll Cardiol 2015;66:1535–7.

5. Shapiro MD, Fazio S. Setting the agenda for preventive cardiology. Circ Res 2017;121:211–3.

6. Castelli WP, Anderson K, Wilson PWF, Levy D. Lipids and risk of coronary heart disease The Framingham Study. Ann Epidemiol 1992;2:23–8.

7. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med 2003;348:383–93.

8. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344:1383–9.

9. Nambi V, Deswal A, Ballantyne CM. Prevention of "failure": Is It a failure of prevention? Circulation 2018;137:106–8.

10. Anitschkow N, Chalatow S. Ueber experimentelle Cholester-insteatose und ihre Bedeutung fuer die Entstehung einiger pathologischer Prozesse. Zentrbl Allg Pathol Pathol Anat 1913;24:1–9.

11. Gofman JW, Glazier F, Tamplin A, Strisower B, De Lalla O. Lipoproteins, coronary heart disease, and atherosclerosis. Physiol Rev 1954;34:589–607.

12. Kresge N, Simoni RD, Hill RL. The biosynthetic pathway for cholesterol: Konrad Bloch. J Biol Chem 2005;280:e7.

13. Goldstein JL, Brown MS. The LDL receptor locus and the genetics of familial hypercholesterolemia. Annu Rev Genet 1979;13:259–89.

14. Goldstein JL, Brown MS. Binding and degradation of low density lipoproteins by cultured human fibroblasts: comparison of cells from a normal subject and from a patient with homozygous familial hypercholesterolemia. J Biol Chem 1974;249:5153–62.

15. The Lipid Research Clinics Coronary Primary Prevention Trial results. I. Reduction in incidence of coronary heart disease. JAMA 1984;251:351–64.

16. The Lipid Research Clinics Coronary Primary Prevention Trial results. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA 1984;251:365–74.

17. Clofibrate and niacin in coronary heart disease. JAMA 1975;231:360–81.

18. Alberts AW, Chen J, Kuron G, et al. Mevinolin: a highly potent competitive inhibitor of hydroxymethylglutaryl-coenzyme A reductase and a cholesterol-lowering agent. Proc Natl Acad Sci U S A 1980;77:3957–61.

19. Abifadel M, Varret M, Rabes JP, et al. Mutations in PCSK9 cause autosomal dominant hypercholesterolemia. Nat Genet 2003;34:154–6.

20. Abifadel M, Elbitar S, El Khoury P, et al. Living the PCSK9 adventure: from the identification of a new gene in familial hypercholesterolemia towards a potential new class of anticholesterol drugs. Curr Atheroscler Rep 2014;16:439.

21. Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. N Engl J Med 2017;376:1713–22.

22. Schwartz GG, Steg PG, Szarek M, et al. Alirocumab and cardiovascular outcomes after acute coronary syndrome. N Engl J Med 2018;379:2097–107.

23. Ray KK, Landmesser U, Leiter LA, et al. Inclisiran in patients at high cardiovascular risk with elevated LDL cholesterol. N Engl J Med 2017;376:1430–40.

24. Bhatt DL, Steg PG, Brinton EA, et al. Rationale and design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial. Clin Cardiol 2017;40:138–48.

25. Nicholls SJ, Lincoff AM, Bash D, et al. Assessment of omega-3 carboxylic acids in statin treated patients with high levels of triglycerides and low levels of high density lipoprotein cholesterol: rationale and design of the STRENGTH trial. Clin Cardiol 2018;41:1281–8.

26. Camejo G. Phase 2 clinical trials with K-877 (pemafibrate): a promising selective PPAR-alpha modulator for treatment of combined dyslipidemia. Atherosclerosis 2017;261:163–4.

27. Bhatt DL, Steg PG, Miller M, et al. Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia. N Engl J Med 2018;380:11–22.

28. Yang X, Lee SR, Choi YS, et al. Reduction in lipoprotein-associated apoC-III levels following volanesorsen therapy: phase 2 randomized trial results. J Lipid Res 2016;57:706–13.

29. Tsimikas S, Viney NJ, Hughes SG, et al. Antisense therapy targeting apolipoprotein(a): a randomised, double-blind, placebo-controlled phase 1 study. Lancet 2015;386:1472–83.

30. Tsimikas S. A Test in context: lipoprotein(a): diagnosis, prognosis, controversies, and emerging therapies. J Am Coll Cardiol 2017;69:692–711.

31. Ridker PM, Everett BM, Thuren T, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. N Engl J Med 2017;377:1119–31.

32. Ridker PM, Everett BM, Pradhan A, et al. Low-dose methotrexate for the prevention of atherosclerotic events. N Engl J Med 2019;380:752–62.

33. The LoDoCo2 Trial: A Randomised Controlled Trial on the Effect of Low Dose Colchicine for Secondary Prevention of Cardiovascular Disease in Patients With Established Stable Coronary Artery Disease. Available at: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=363771. Accessed February 21, 2019.

34. Colchicine Cardiovascular Outcomes Trial (COLCOT). Available at: https://clinicaltrials.gov/ct2/show/NCT02551094. Accessed March 11, 2019.

35. American Diabetes A. Standards of medical care in diabetes-2011. Diabetes Care 2011;34 Suppl 1:S11–61.

36. Grundy SM, Benjamin IJ, Burke GL, et al. Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation 1999;100:1134–46.

37. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837–53.

38. Dluhy RG, McMahon GT. Intensive glycemic control in the ACCORD and ADVANCE trials. N Engl J Med 2008;358:2630–3.

39. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. N Engl J Med 2007;356:2457–71.

40. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015;373:2117–28.

41. Inzucchi SE, Kosiborod M, Fitchett D, et al. Improvement in cardiovascular outcomes with empagliflozin is independent of glycemic control. Circulation 2018;138:1904–7.

42. Mahaffey KW, Neal B, Perkovic V, et al. Canagliflozin for primary and secondary prevention of cardiovascular events: results from the CANVAS program (Canagliflozin Cardiovascular Assessment Study). Circulation 2018;137:323–34.

43. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2019;380:347–57.

44. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2016;375:311–22.

45. Hernandez AF, Green JB, Janmohamed S, et al. Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial. Lancet 2018;392:1519–29.

46. Vaduganathan M, Sathiyakumar V, Singh A, et al. Prescriber patterns of SGLT2i after expansions of U.S. Food and Drug Administration labeling. J Am Coll Cardiol 2018;72:3370–2.

47. Das SR, Everett BM, Birtcher KK, et al. 2018 ACC expert consensus decision pathway on novel therapies for cardiovascular risk reduction in patients with type 2 diabetes and atherosclerotic cardiovascular disease: a report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol 2018;72:3200–23.

48. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. J Am Coll Cardiol 2014;63:2985–3023.

49. Kang JG, Park CY. Anti-obesity drugs: a review about their effects and safety. Diabetes Metab J 2012;36:13–25.

50. Pareek M, Schauer PR, Kaplan LM, Leiter LA, Rubino F, Bhatt DL. Metabolic surgery: weight loss, diabetes, and beyond. J Am Coll Cardiol 2018;71:670–87.

51. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med 2012;366:1567–76.

52. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes-3-year outcomes. N Engl J Med 2014;370:2002–13.

53. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes. N Engl J Med 2017;376:641–51.

54. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. Lancet 2015;386:964–73.

55. Vest AR, Heneghan HM, Agarwal S, Schauer PR, Young JB. Bariatric surgery and cardiovascular outcomes: a systematic review. Heart 2012;98:1763–77.

56. Zhou X, Yu J, Li L, et al. Effects of bariatric surgery on mortality, cardiovascular events, and cancer outcomes in obese patients: systematic review and meta-analysis. Obes Surg 2016;26:2590–601.

57. Benotti PN, Wood GC, Carey DJ, et al. Gastric bypass surgery produces a durable reduction in

cardiovascular disease risk factors and reduces the long-term risks of congestive heart failure. J Am Heart Assoc 2017;6:e005126.

58. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2018;71:e127–248.

59. 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:e67–492.

60. Group TSR. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015;373:2103–16.

61. Flint AC, Conell C, Ren X, et al. Effect of systolic and diastolic blood pressure on cardiovascular outcomes. N Engl J Med 2019;381:243–51.

62. Muntner P, Carey RM, Gidding S, et al. Potential U.S. population impact of the 2017 ACC/AHA high blood pressure guideline. J Am Coll Cardiol 2018;71:109–18.

63. Unger T, Paulis L, Sica DA. Therapeutic perspectives in hypertension: novel means for renin-angiotensin-aldosterone system modulation and emerging device-based approaches. Eur Heart J 2011;32:2739–47.

64. Oparil S, Schmieder RE. New approaches in the treatment of hypertension. Circ Res 2015;116:1074–95.

65. Lobo MD, Sobotka PA, Pathak A. Interventional procedures and future drug therapy for hypertension. Eur Heart J 2017;38:1101–11.

66. Gaziano JM, Brotons C, Coppolecchia R, et al. Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial. Lancet 2018;392:1036–46.

67. Group ASC, Bowman L, Mafham M, et al. Effects of aspirin for primary prevention in persons with diabetes mellitus. N Engl J Med 2018;379:1529–39.

68. McNeil JJ, Wolfe R, Woods RL, et al. Effect of aspirin on cardiovascular events and bleeding in the healthy elderly. N Engl J Med 2018;379:1509–18.

69. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;74:1376–414.

70. Abdelaziz HK, Saad M, Pothineni NVK, et al. Aspirin for primary prevention of cardiovascular events. J Am Coll Cardiol 2019;73:2915–29.

71. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2012;60:e44–164.

72. Johnston A, Jones WS, Hernandez AF. The ADAPTABLE trial and aspirin dosing in secondary prevention for patients with coronary artery disease. Curr Cardiol Rep 2016;18:81.

73. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2016;68:1082–115.

74. Steg PG, Bhatt DL, Simon T, et al. Ticagrelor in patients with stable coronary disease and diabetes. N Engl J Med 2019 Sep 1 [E-pub ahead of print].

75. Eikelboom JW, Connolly SJ, Bosch J, et al. Rivaroxaban with or without aspirin in stable cardiovascular disease. N Engl J Med 2017;377:1319–30.

76. GBD 2013 DALYs and HALE Collaborators, Murray CJ, Barber RM, Foreman KJ, et al. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. Lancet 2015;386:2145–91.

77. Barua RS, Ambrose JA, Eales-Reynolds LJ, DeVoe MC, Zervas JG, Saha DC. Dysfunctional endothelial nitric oxide biosynthesis in healthy smokers with impaired endothelium-dependent vasodilatation. Circulation 2001;104:1905–10.

78. Barua RS, Sharma M, Dileepan KN. Cigarette smoke amplifies inflammatory response and atherosclerosis progression through activation of the H1R-TLR2/4-COX2 axis. Front Immunol 2015;6:572.

79. Barua RS, Sy F, Srikanth S, et al. Acute cigarette smoke exposure reduces clot lysis-association between altered fibrin architecture and the response to t-PA. Thromb Res 2010;126:426–30.

80. Barua RS, Sy F, Srikanth S, et al. Effects of cigarette smoke exposure on clot dynamics and fibrin structure: an ex vivo investigation. Arterioscler Thromb Vasc Biol 2010;30:75–9.

81. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. J Am Coll Cardiol 2004;43:1731–7.

82. Morris PB, Ference BA, Jahangir E, et al. Cardiovascular effects of exposure to cigarette smoke and electronic cigarettes: clinical perspectives from the Prevention of Cardiovascular Disease Section Leadership Council and Early Career Councils of the American College of Cardiology. J Am Coll Cardiol 2015;66:1378–91.

83. Rigotti NA, Clair C. Managing tobacco use: the neglected cardiovascular disease risk factor. Eur Heart J 2013;34:3259–67.

84. Gopal DM, Kalogeropoulos AP, Georgiopoulou VV, et al. Cigarette smoking exposure and heart failure risk in older adults: the Health, Aging, and Body Composition Study. Am Heart J 2012;164:236–42.

85. D'Ascenzo F, Bollati M, Clementi F, et al. Incidence and predictors of coronary stent thrombosis: evidence from an international collaborative meta-analysis including 30 studies, 221,066 patients, and 4276 thromboses. Int J Cardiol 2013;167:575–84.

86. Hermanson B, Omenn GS, Kronmal RA, Gersh BJ. Beneficial six-year outcome of smoking cessation in older men and women with coronary artery disease. Results from the CASS registry. N Engl J Med 1988;319:1365–9.

87. Meyers DG, Neuberger JS, He J. Cardiovascular effect of bans on smoking in public places: a systematic review and meta-analysis. J Am Coll Cardiol 2009;54:1249–55.

88. Karnath B. Smoking cessation. Am J Med 2002;112:399–405.

89. Lightwood JM, Glantz SA. Short-term economic and health benefits of smoking cessation: myocardial infarction and stroke. Circulation 1997;96:1089–96.

90. Barua RS, Rigotti NA, Benowitz NL, et al. 2018 ACC expert consensus decision pathway on tobacco cessation treatment: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol 2018;72:3332–65.

91. Khambhati J, Allard-Ratick M, Dhindsa D, et al. The art of cardiovascular risk assessment. Clin Cardiol 2018;41:677–84.

92. 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:e285–350.

93. Hecht H, Blaha MJ, Berman DS, et al. Clinical indications for coronary artery calcium scoring in asymptomatic patients: expert consensus statement from the Society of Cardiovascular Computed Tomography. J Cardiovasc Comput Tomogr 2017;11:157–68.

94. Nasir K, Rubin J, Blaha MJ, et al. Interplay of coronary artery calcification and traditional risk factors for the prediction of all-cause mortality in asymptomatic individuals. Circ Cardiovasc Imaging 2012;5:467–73.

95. Silverman MG, Blaha MJ, Krumholz HM, et al. Impact of coronary artery calcium on coronary heart disease events in individuals at the extremes of traditional risk factor burden: the Multi-Ethnic Study of Atherosclerosis. Eur Heart J 2014;35:2232–41.

96. Blankstein R, Budoff MJ, Shaw LJ, et al. Predictors of coronary heart disease events among asymptomatic persons with low low-density lipoprotein cholesterol MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol 2011;58:364–74.

97. Mortensen MB, Fuster V, Muntendam P, et al. Negative risk markers for cardiovascular events in the elderly. J Am Coll Cardiol 2019;74:1–11.

98. Nasir K, Bittencourt MS, Blaha MJ, et al. Implications of coronary artery calcium testing among statin candidates according to American College of Cardiology/American Heart Association Cholesterol Management Guidelines: MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol 2015;66:1657–68.

99. Bittencourt MS, Blankstein R, Blaha MJ, et al. Implications of coronary artery calcium testing on risk stratification for lipid-lowering therapy according to the 2016 European Society of Cardiology recommendations: the MESA study. Eur J Prev Cardiol 2018;25:1887–98.

100. Gupta A, Wang Y, Spertus JA, et al. Trends in acute myocardial infarction in young patients and differences by sex and race, 2001 to 2010. J Am Coll Cardiol 2014;64:337–45.

101. Chow BJ, Small G, Yam Y, et al. Prognostic and therapeutic implications of statin and aspirin therapy in individuals with nonobstructive coronary artery disease: results from the CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter registry) registry. Arterioscler Thromb Vasc Biol 2015;35:981–9.

102. Hulten E, Bittencourt MS, Singh A, et al. Coronary artery disease detected by coronary computed tomographic angiography is associated with intensification of preventive medical therapy and lower low-density lipoprotein cholesterol. Circ Cardiovasc Imaging 2014;7:629–38.

103. Mitchell JD, Fergestrom N, Gage BF, et al. Impact of statins on cardiovascular outcomes following coronary artery calcium scoring. J Am Coll Cardiol 2018;72:3233–42.

104. Corti R, Fuster V. Imaging of atherosclerosis: magnetic resonance imaging. Eur Heart J 2011;32:1709–1719b.

105. Naslund U, Ng N, Lundgren A, et al. Visualization of asymptomatic atherosclerotic disease for optimum cardiovascular prevention (VIPVIZA): a pragmatic, open-label, randomised controlled trial. Lancet 2019;393:133–42.

106. Saeed A, Dabhadkar K, Virani SS, Jones PH, Ballantyne CM, Nambi V. Cardiovascular disease prevention: training opportunities, the challenges, and future directions. Curr Atheroscler Rep 2018;20:35.

107. Smith SC Jr., Bittner V, Gaziano JM, et al. COCATS 4 Task Force 2: training in preventive cardiovascular medicine. J Am Coll Cardiol 2015;65:1754–62.

108. Blackwell T, Cassel C, Duffy FD, et al. Final report of the Committee on Recognizing New and Emerging Disciplines in Internal Medicine (NEDIM). 2006. Available at: https://www.abim.org/~/media/ABIM%20Public/Files/pdf/report/nedim-2-report.pdf. Accessed March 20, 2019.

109. Eckel RH, Syrek R. Considering a Cardiometabolic Subspecialty. July 31, 2018. Medscape. Available at: https://www.medscape.com/viewarticle/899864. Accessed April 9, 2019.

110. Eckel RH, Blaha MJ. Cardiometabolic medicine: a call for a new subspeciality training track in internal medicine. Am J Med 2019;132:788–90.

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