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New American Heart Association/American College of Cardiology Guidelines on Cardiovascular Risk: When Will Fitness Get the Recognition It Deserves?

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During the American Heart Association (AHA) Scientific Sessions in November 2013, the AHA and the American College of Cardiology (ACC) jointly released new guidelines for the prevention and treatment of coronary artery disease (CAD). The guidelines focused on the assessment of cardiovascular risk[1] and the treatment of blood lipids[2] and received a great deal of attention from both the media and professional journals. These organizations are among the most experienced and qualified to develop guidelines, and their guidelines and scientific statements set the standard for clinical practice. Most of this attention focused on an updated cardiovascular *risk calculator*, using an equation developed from community-based populations that includes established risk factors such as race, sex, age, total cholesterol level, blood pressure, high-density lipoprotein cholesterol level, diabetes mellitus, and smoking status. The risk calculator is designed to estimate the 10-year risk of myocardial infarction and stroke among individuals aged 40 to 79 years. Tools such as these are valuable in that they allow a health care professional to roughly estimate a patient's likelihood of a cardiovascular event and to direct treatment accordingly.

With the release of the guidelines, a vigorous debate among medical professionals and the lay press immediately ensued regarding the effect of the guidelines on the use of medications to treat heart disease. The new guidelines recommend statins for people with a *lower* risk of cardiovascular disease (CVD) than in previous guidelines (a 7.5% risk during 10 years compared with a 10-year risk of 10% to 20% according to the previous guidelines) and for those at risk for stroke. In addition, they eliminate the earlier criterion that a patient's low-density lipoprotein cholesterol (LDL-C) level be at or above a certain level to warrant treatment, with the exception of those with extremely high LDL-C levels (>190 mg/dL [to convert to mmol/L, multiply by 0.0259). Although statins are no longer recommended for patients taking the drugs only to lower their LDL-C level, eliminating the LDL-C criterion will mean a vast increase in statin prescriptions overall, including millions of individuals who have no heart disease but meet the 10-year risk criterion of 7.5%. Several reports estimated that implementation of these guidelines will increase the number of healthy individuals for whom statins are recommended by as much as 70%.[3]

During the past 2 decades, statins have been reported to reduce the risk of cardiovascular events by roughly 20% to 25%.[4] However, this decrease in risk is highly dependent on the degree of risk in the population being considered. Individuals without a diagnosis of CVD would lower their yearly risk of having a cardiac event from approximately 1.8% to 1.4% if they take a statin. This 0.4% reduction in risk, when balanced against the cost of taking statins (estimated to be up to $1 per day per person for nongenerics[5]) and the total cost of statin use in the United States (approximately $20 billion annually), not surprisingly caused significant consternation among some health care professionals. Others have calculated that the new guidelines considerably overestimate the 10-year risk of cardiovascular events. After the release of the new guidelines, Ridker and Cook[6] from Brigham and Women's Hospital in Boston, Massachusetts, calculated the 10-year risks of cardiac events in 3 large-scale primary prevention cohorts: The Women's Health Study, the Physician's Health Study, and the Women's Health Initiative Observational Study.

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They reported that the new algorithm overestimated risk by 75% to 150%.

The guidelines generated another spirited controversy relevant to preventive medicine. Although most clinicians and the lay press focused on the controversy related to the potential overuse of statins, what frustrated many in the exercise and prevention field is the fact that what is arguably the most powerful predictor of risk, fitness, was excluded from the new risk calculator. More than 20 years ago, the AHA designated physical inactivity as the fourth *primary* risk factor for CVD, elevating it from *secondary* risk factor status.[7] There have been numerous recent calls for the recognition of fitness as a risk factor to be routinely considered along with the conventional factors such as smoking, hypertension, and lipid abnormalities. However, despite numerous epidemiologic studies reporting the critical role of fitness and physical activity patterns in predicting risk of adverse health outcomes, only a minority of health care professionals counsel patients on physical activity.[8,9] The concept that people without CVD might lower their risk of a cardiac event by four-tenths of a percentage point by taking a statin while an individual's fitness or physical activity pattern is not considered has not sat well with many health care professionals. A number of provocative questions have been raised, including the following:

1. What would an individual's risk be if he or she did not take statins and instead quit smoking or started exercising?
2. Is lifelong use of statins a better investment of our health care dollars than a few months of sessions with an exercise physiologist and/or a nutritionist to encourage healthier nutrition, weight loss, and an improvement in fitness?
3. When will fitness gain legitimacy as a risk factor as deserving of consideration as hypertension or hyperlipidemia? When will it be fully incorporated into the health care paradigm, as numerous epidemiologic studies[10] and commentaries from researchers[9,11-14] suggest that it should?

Regarding the first question, studies have found that in high-risk individuals, statin therapy reduces the risk of future cardiac events. For example, 3 recent meta-analyses reported approximately 20% to 25% reductions in cardiac events after statin therapy, and the results were similar for men and women.[4,15,16] The number needed to treat (NNT) to prevent one death with statin therapy during 5 years in low-risk individuals has been reported to be as high as 1000,[3] and the 5-year NNT to prevent a cardiac event (myocardial infarction or stroke) is approximately 140.[17] Among higher-risk populations, the NNT is much lower but ranges widely (10 to approximately 100).[18,19] The level of evidence in support of statin use from clinical trial data is undeniably strong. However, well-documented adverse effects of statins include a higher incidence of diabetes, liver damage, muscle pain, inflammation, myopathy, and an attenuation of the effects of exercise training.[17] The high NNT and potential for harm support the contention that statins are not appropriate for low-risk (5-year risk of <10%) individuals.[17,18] Moreover, many have expressed the view that statins provide false reassurances that may discourage patients from making the lifestyle changes that reduce cardiovascular disease.[3,20] Physicians and patients have been taught to be overly focused on lipids rather than behavior modification to prevent heart disease, and statins may give the illusion of protection to many patients who might be better served by a healthier diet, incorporating a modest amount of exercise into each day, and quitting smoking.

On the basis of data from major trials, such as the Nurses Health Study,[21] the Interheart Study,[22] and estimates from the World Health Organization,[23] 80% or more of CVD cases can be attributed to smoking, lack of exercise, and an unhealthy diet. Undeniably, more active individuals have been consistently found in many epidemiologic studies to have significantly lower cardiovascular event rates than those who are habitually inactive. There are many examples in the recent literature, and a meta-analysis by Nocon et al[24] is reflective of these studies. On the basis of an analysis of nearly 900,000 participants, physically active individuals had pooled risk reductions of 35% for cardiovascular mortality and 33% for all-cause mortality when compared with inactive individuals. As documented in a recent meta-analysis and review of 305 trials involving more than 339,000 individuals by Naci and Ioannidis,[25] exercise was statistically

as effective as drug interventions for the secondary prevention of coronary heart disease and prediabetes. Among patients who had experienced a stroke, physical activity interventions were more effective than drug treatment. The interaction between statin use and cardiorespiratory fitness was recently explored by Kokkinos and coworkers[26] among more than 10,000 patients with lipid abnormalities in the Veterans Exercise Testing Study. Both statin use and higher fitness levels independently lowered risk of mortality. The combination of statin treatment and an exercise capacity of greater than 5 metabolic equivalents (METs), a relatively modest fitness level, lowered mortality risk substantially more than either alone. Individuals in the highest quartile of fitness who were taking statins had a 70% lower mortality rate than the least fit individuals who were taking statins. Thus, data such as these suggest that exercise is an intervention that is at least equivalent to most other interventions for the prevention of chronic disease.

The second question, whether statin use is cost-effective, is more complex; cost-effectiveness is highly dependent on how it is defined, the group studied, and a number of assumptions. In high-risk patients, low-cost (generic) statins have generally been considered to be cost-effective.[27,28] It remains unclear whether statin use is cost-effective for lower-risk groups, such as the broader population of individuals who might receive statins under the new guidelines.[3] Cost-effectiveness will also be affected as more statins become generic. The increase in the use of statins during the past 2 decades and the debate regarding their cost-effectiveness has occurred during a time in which there has been a plethora of studies on the cost-effectiveness of physical activity interventions. Many of these studies have involved short-term (<1-year) employee health promotion programs, and although there are biases to be considered (eg, participation bias in which those who choose to participate are healthier than those who do not), these studies are consistent in demonstrating that health care expenditures are lower among more active individuals.[29,30] Pronk et al,[31] for example, reported 4.7% lower health care charges per day per week that an individual was active. Our group observed a 6% reduction in 1-year health care costs per tertile of physical activity and roughly $1 lower health care costs per kilocalorie expended per week (or approximately $50,000 lower costs per year among patients meeting the widely recommended 1000 kcal/wk activity threshold).[32]

Surprisingly, few data are available relating health care costs to objective measures of fitness. Bachman et al[33] studied more than 20,000 middle-aged individuals from the Cooper Center Longitudinal Study and reported that the fittest 2 quintiles had 38% lower health care costs than the least fit individuals during roughly 20 years of follow-up. In a study among veterans, fitness level was found to be the strongest predictor of health care costs among clinical, demographic, and exercise test variables during the year subsequent to an exercise test.[34] In addition, a 5.4% reduction in total health care costs per MET achieved was observed. Thus, in addition to its effect on health outcomes, improving fitness through physical activity should be encouraged by health care professionals, health care systems, and through worksite programs for its potential to lower health care costs. Given the well-documented cost-effectiveness of physical activity interventions, one wonders why a patient can be referred for cardiac imaging, subsequent coronary intervention, and long-term drug treatment while an insurance company covers the costs, yet the same insurer will not pay for an appointment with an exercise professional.

The third question addresses the recognition of fitness as a risk factor and why it lacks the attention given to the traditional risk factors such as smoking, hypertension, lipid abnormalities, and others. During the past 2 decades, a wealth of studies have documented that even small changes in fitness yield major health outcome benefits.[7,9-14] The strength of the association between fitness and both cardiovascular and all-cause mortality was recently underscored in an eloquent meta-analysis by Kodama et al.[9] Data were extracted from 33 studies and nearly 103,000 participants. Compared with patients in the most fit tertile, those with low fitness had a 70% higher risk of all-cause mortality and a 56% higher risk of cardiovascular mortality. Across all studies, 13% and 15% reductions in cardiovascular and all-cause mortality, respectively, were observed per MET achieved. An important and consistent finding in these studies is the fact that the greatest health outcome benefits are observed between the least

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fit and the next least fit group; lesser improvements in health outcomes occur between individuals who are in the moderate- to high-fit groups. Stated differently, the health benefits of fitness are most evident in the low end of the fitness spectrum. Many recent studies have also demonstrated that low fitness is a stronger predictor of risk of adverse outcomes than the traditional risk factors.[9,12,14] Despite these observations, the importance of fitness in the risk paradigm has historically received inadequate attention in cardiovascular medicine because of the tendency to focus on the ST segment and the potential need for revascularization.[9,12]

Lifestyle behaviors, such as tobacco use, poor diet, and physical inactivity, are major determinants of disease and death in the United States, yet these have historically received little attention from our health care system in terms of preventing them in the first place. The Affordable Care Act of 2010 includes federally mandated preventive services for adults that incorporate counseling on health and wellness issues, including physical activity. Although the Affordable Care Act faces challenges in terms of how federal, state, and local policymakers allocate new funding, these mandated preventive services represent a paradigm shift in the US health care system and have the potential to be an important means to reverse the epidemic of physical inactivity. It is imperative that health care professionals, health care systems, and patients gain a better understanding of the risks of being sedentary and the importance of incorporating exercise into the health care paradigm for the prevention and treatment of chronic disease. The recent debate regarding the new AHA/ACC risk calculator may be just the latest example of how the US health care system does not appropriately value fitness and physical activity,[9,11-14] but the debate has provided another opportunity to educate health care professionals and the public about their importance.

Abbreviations and Acronyms: **ACC** = American College of Cardiology; **AHA** = American Heart Association; **CAD** = coronary artery disease; **CVD** = cardiovascular disease; **LDL-C** = low-density lipoprotein cholesterol; **MET** = metabolic equivalent; **NNT** = number needed to treat

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