Dyslipidemia, hypertension, and diabetes mellitus have been appropriately highlighted as established predictors of cardiovascular disease. These risk factors have become preeminent targets for influencing cardiovascular risk; their assessment, treatment, and monitoring are major emphases of clinical care, research investigation, treatment guidelines, organization position papers, and measures of physician and hospital performance. Notably, lifestyle risk factors, including dietary habits, physical inactivity, smoking, and adiposity, strongly influence the established cardiovascular risk factors and also affect novel pathways of risk such as inflammation/oxidative stress, endothelial function, thrombosis/coagulation, and arrhythmia. Furthermore, modest alterations of these lifestyle risk factors are achievable and have substantial effects on cardiovascular risk. Thus, basic lifestyle habits should be considered fundamental risk factors for cardiovascular disease. Although efforts to combat established and novel risk factors with pharmacological treatments are important and should continue, we call for a systematic rebalancing of current research, clinical care, and policy efforts to focus more on lifestyle. The rising costs of healthcare and the epidemics of overweight and obesity highlight the inadequacies of our current strategy. Substantially more resources should be directed toward research on lifestyle risk factors, their determinants, and effective interventions to change them. The clinical evaluation and treatment of dietary, physical activity, and smoking habits must become as routine and familiar as assessment of blood pressure, cholesterol, and glucose levels. Major policy initiatives and reimbursement guidelines must also be rebalanced to emphasize lifestyle risk factors.

Established Cardiovascular Risk Factors
Cardiovascular diseases are leading causes of death and disability among men and women in nearly all nations. Identification of persons at higher or lower risk for cardiovascular events is important to facilitate effective use of resources and interventions to reduce disease burden among individuals and in society. Each of the established risk factors for cardiovascular disease—age, gender, dyslipidemia, hypertension, diabetes mellitus, and smoking—have been appropriately highlighted as useful for prediction of risk.2–4 Integration of these factors into risk scores (eg, the Framingham Risk Score) provides quantitative prediction of an individual’s future risk of coronary heart disease (CHD),4 generalizable across different populations after calibration of absolute risks.5–10

From Prediction to Treatment
Dyslipidemia, hypertension, and diabetes mellitus were initially identified because they predicted cardiovascular events. Prediction models make no assumptions (and allow no inferences) about the presence or extent of confounding, magnitude of causal effects, or hierarchy of variables along causal pathways. For instance, although diabetes mellitus and elevated glucose levels clearly predict CHD risk, lowering of glucose by drug treatment generally has not produced anticipated reductions in CHD events,11,12,12a suggesting that elevated glucose may at least partly signify more proximal pathology (eg, adipocyte stress and dysfunction) that increases macrovascular risk. Conversely, a major advance in medicine has been confirmation in pharmaceutical trials that blood pressure and blood lipids are in the casual pathway for cardiovascular events (although some benefits of statins may also result from nonlipid effects).13–17 Such results do not clarify whether focus on blood pressure and blood lipid levels is either the most efficacious or cost-effective means to reduce risk. Nevertheless, measurement and treatment of blood lipids, blood pressure, and glucose levels have become the major emphases for cardiovascular risk reduction. The strong influence of pharmaceutical dollars and advertising in this process cannot be overlooked.18–21 Cholesterol-lowering and blood pressure–lowering medications are consistently among the world’s top-selling drugs.22 Assessment and pharmacological treatment of elevated blood pressure, cholesterol, and glucose levels have become standards of cardiovascular care and the major emphases of practice guidelines, organization position papers, healthcare quality indicators, and reimbursement standards.23–28

Lifestyle Risk Factors
The emphasis on treatment and control of the established cardiovascular risk factors, although not optimal in execu-
Figure 1. The relations of lifestyle, established and novel risk factors, and cardiovascular disease. Assessment and treatment of dyslipidemia, hypertension, and diabetes are major foci of clinical care, practice guidelines, performance measures, and scientific research. These established cardiovascular risk factors are strongly influenced by lifestyle, including dietary behaviors, physical inactivity, smoking, and adiposity. Adiposity itself is largely a result of poor diet (excess calories) and inactivity. Lifestyle risk factors also influence disease risk via effects on other novel risk factors such as endothelial function, inflammation/oxidative stress, thrombosis/coagulation, arrhythmia, and other pathways. These basic lifestyle habits—poor diet, physical inactivity, and smoking—are thus the most proximal risk factors for cardiovascular disease.

The harm of smoking and the tremendous benefits of smoking prevention and cessation are well established. Quitting smoking re-
duces total mortality by approximately one third, a remarkable benefit. Declines in smoking have substantially reduced cardiovascular events in some populations, but many individuals continue to smoke. Furthermore, smoking and smoking-related deaths are increasing in many subgroups and regions. Additional research and policy initiatives are urgently needed to improve current practices and develop new interventions and policies to reduce smoking.

Benefits of physical activity are remarkable. Physical activity raises high-density lipoprotein cholesterol, lowers low-density lipoprotein cholesterol and triglycerides, lowers blood pressure, improves fasting and postprandial glucose-insulin homeostasis, induces and maintains weight loss, improves psychological well-being, and likely lowers inflammation, improves endothelial function, and facilitates smoking cessation. Consistent with these pleiotropic benefits, physical activity and fitness are associated with 30% to 50% lower risk of cardiovascular events. In patients with established cardiovascular disease, physical activity reduces angina symptoms, benefits heart failure, decreases claudication, and lowers mortality after myocardial infarction. Herculean efforts are not required; great benefit is achieved with modest activity, eg, 30 minutes of brisk walking on most days.

Dietary habits also powerfully affect cardiovascular risk. In randomized trials, dietary habits affect both established and many other intermediary risk factors. Modest consumption of oily fish (1 to 2 servings per week) reduces CHD death by 36%, with 17% reduction in total mortality in randomized controlled trials of fish oil in higher-risk populations. Prospective studies indicate consistent and substantial reductions in cardiovascular risk related to lower trans fat consumption; consumption of whole grains, legumes, and cereal fiber; and consumption of fruits and vegetables. Other dietary habits that may lower cardiovascular risk include modest consumption of nuts, alcohol, plant-derived ω-3 fatty acids, and dairy products; and replacement of saturated fat or refined carbohydrates with unsaturated ω-6 polyunsaturated or monounsaturated fats.

For many lifestyle habits, the impact on health of a single behavioral change—lifestyle monotherapy—are substantial. In combination, changes in lifestyle habits produce even greater benefits. In a secondary prevention trial, advice to consume a Mediterranean-type diet (vegetables, fruits, fish, chicken, grains, canola margarine) reduced risk of myocardial infarction or cardiac death by 72% over a 4-year follow-up. In another trial, modest lifestyle recommendations (advice to consume a healthy low-calorie diet and be moderately active, such as walking briskly 20 min/d) reduced incidence of diabetes mellitus by 58% compared with placebo and by 39% compared with metformin. These effects on incident diabetes substantially underestimate the superiority of the lifestyle intervention for reducing cardiovascular risk: Although both lifestyle and metformin lowered glucose levels (lesssening the nominal diagnosis of diabetes mellitus), only the lifestyle intervention improved multiple other established cardiovascular risk factors related to inactivity, adiposity, and poor dietary habits.

On the basis of population-wide benefits and minimization of adverse drug effects, changes in lifestyle may be most important for primary prevention. Conversely, many lifestyle habits (both good and bad) may confer similar relative effects for secondary prevention, which would translate into greater absolute risk differences. All lifestyle recommendations do not affect cardiovascular risk equally because of lower efficacy of the specific chosen recommendations (eg, decreasing total fat intake, ineffective mode of delivery, or competing environmental or societal factors). In some cases, the quality of evidence for benefits of some cardiovascular drugs exceeds that for some lifestyle changes. This is often a result of discrepancies in the sizes and numbers of large randomized trials that have evaluated the effects of drugs and devices, rather than basic lifestyle habits, on cardiovascular events, driven by both pharmaceutical research and profits and the ongoing clinical and scientific focus on drug development.

Changing Behavior

It is often argued that strategies emphasizing lifestyle behaviors may be less effective or impractical compared with drug-based approaches. Such beliefs, together with powerful financial incentives for drug development, encourage polypharmaceutical strategies that target established and novel risk factors. However, considerable evidence demonstrates that lifestyle behaviors can be changed. For decades, cigarette and food companies have altered our behavior with great aplomb. Emphasizing behavioral research, they have perfected methods for behavior modification and directed our lifestyle choices and habits highly effectively. Although public health programs and expertise to promote healthy lifestyles lag far behind those of industry, even basic campaigns can have a significant impact. Major gaps remain, but strategies to lessen smoking in the United States have been effective, reducing per capita tobacco use by nearly two thirds since the 1950s. Campaigns promoting use of seatbelts, bike helmets, and sunscreen have also been effective. Complex population behaviors, such as dietary habits, can also be modified. From 1977 to 2000, a major focus of US dietary guidelines was reduction of total dietary fat, and during this time, average US fat consumption declined from 36.4% to 32.8% of calories. Dietary guidelines also emphasized carbohydrate consumption (the food pyramid base), which increased from 44.3% to 50.3% of calories. Although benefits of these particular dietary changes can be debated (concurrently, total calories increased from 2000 to 2250 kcal/d), population-wide behavioral changes are clearly achievable.

Community-based trials have been variably successful at changing lifestyle habits, and additional research is clearly needed to determine optimal strategies for behavior change. Nevertheless, several randomized controlled trials have demonstrated that individual-targeted programs can modify lifestyle behaviors and improve a wide range of intermediary cardiovascular risk factors. For example, in a trial among 5145 diabetics, lifestyle advice lowered systolic blood pressure, diastolic blood pressure, triglycerides, fasting glucose, hemoglobin A1c, and proteinuria; in-
creased high-density lipoprotein cholesterol; increased weight loss and physical fitness; and reduced use of diabetic, antihypertensive, and lipid-lowering medications.\textsuperscript{113}

Adherence to both lifestyle advice and drug therapy is imperfect. In the Women’s Health Initiative, not all participants met the dietary goal (<20% energy from fat), but fat consumption was still substantially lower in the dietary advice arm at both 1 year (24.3% versus 35.1% energy) and 6 years (28.8% versus 37.0% energy).\textsuperscript{77} In this same trial, 40% of women stopped the study drug (including placebo) at an average 5.2 years of follow-up\textsuperscript{104} and 54% at an average 6.8 years of follow-up.\textsuperscript{105} At the end of the Diabetes Prevention Project, 58% of the lifestyle group maintained the physical activity goal (≥2.5 h/wk), 38% achieved and maintained the weight loss goal (≥7% weight loss), and 67% were ≥80% adherent to drug therapy (the proportion fully adherent was not reported).\textsuperscript{55} The proportion of individuals compliant (≥80% adherence) with lipid-lowering or antihypertensive drugs typically ranges from 65\% to 85\% in clinical trials to <50\% in clinical practice.\textsuperscript{106–108} Direct evidence comparing relative adherence to modest lifestyle changes versus lifelong use of drugs is scant; improving adherence to both lifestyle and drug interventions should be a major goal of future research.

In the past 2 decades, American dietary habits have changed substantially, including increased daily consumption of total food, high-energy-density products, per meal food quantity and calories, meals prepared outside the home, and sugar-sweetened beverages.\textsuperscript{109–111} At this same time, the prevalence of overweight and obesity has increased dramatically.\textsuperscript{112,113} These trends indicate our capacity for rapid and significant behavior change. To reverse these trends, we must first understand whether they have resulted from innumerable minor or a handful of major individual, environmental, and societal factors. Investigating the determinants of these behavior changes and the means to reverse them should be a chief priority of our scientific inquiry.

The Need for Balance

Even with optimal lifestyle, some age- and genetic-related increases in metabolic risk factors will occur. Thus, attention to such risk factors is important, and pharmacological therapies will still be needed in certain individuals, particularly with advancing age. However, sufficient focus on lifestyle risks would substantially reduce the numbers and delay the onset of individuals needing drug treatments as well as lower the incidences of cardiovascular disease, diabetes mellitus, and obesity. Policy, clinical care, and research efforts are currently imbalanced. For example, gaps in treatment are often identified on the basis of patients not meeting guidelines for blood pressure, cholesterol, or glucose levels but rarely on the basis of physical activity, weight, or dietary habits. Patients are often concerned and ask their doctor about their blood pressure and cholesterol levels, whereas smoking, activity, and dietary habits are insufficiently discussed. The emphasis on metabolic risks is also reflected in research (Figure 2). These imbalances are driven by several factors, including historical tradition; the relative ease of measuring and writing prescriptions for blood pressure, cholesterol, or glucose levels compared with assessing lifestyle; the impression that modest lifestyle changes are more difficult to sustain than lifelong use of drugs; and compelling financial interests that leverage research and care delivery on the basis of drug treatments of established or novel risk factors. Notably, little direct financial incentive has existed to investigate or promote lifestyle behaviors to prevent or treat disease and reduce the burden of established risk factors. Ironically, a large proportion of healthcare expenditures, including costs to individuals, businesses, and society, is attributable to poor lifestyle behaviors,\textsuperscript{114–117} and these costs are lowered by initiatives that promote healthy lifestyles.\textsuperscript{118}

Current research, clinical, and policy efforts must each be systematically rebalanced. Substantial resources should be directed toward investigating effects of lifestyle risk factors,
their personal and environmental determinants, and the effective interventions to change them, integrating influences of psychosocial, educational, neighborhood, and economic conditions. Continued attention to other areas of research, such as established and novel metabolic risk factors, drug and device development, genetics, and molecular biology, is clearly important and should complement lifestyle-related investigation. Potential novel lifestyle determinants (eg, sleep duration) should also receive more attention.

In clinical care, the evaluation, treatment, and follow-up of dietary, physical activity, and smoking habits must become as routine, expected, and familiar, for both provider and patient, as assessment of blood pressure, cholesterol, and glucose levels. Simple and accessible tools for healthcare providers to accomplish this must be developed and validated. Attention to and success of such interventions must be appropriately reimbursed and form the core of practice guidelines and quality care standards. On the basis of current evidence, emphasizing a few “golden rules” may be most efficient, eg, walk, bike, or swim for 30 minutes most days; consume fish, whole grains/legumes, fruits, vegetables, and nuts; always eat small portion sizes; avoid trans fats, sugared beverages, and highly processed foods; and, without question, do not smoke.

Local, state, and federal policy initiatives must also emphasize lifestyle risk factors. Producing lifestyle changes through individual initiative by a knowledgeable population is apt to be most effective when government action encourages physical activity back into daily life, alters the national diet by creating incentives to provide unprocessed foods and healthier packaged foods, and abolishes cigarette smoking. Efforts to combat established risk factors should continue, while at the same time redrawing the framework so that lifestyle risk factors are principal considerations when cardiovascular disease is contemplated by the public, patients, clinicians, researchers, and policy makers. In addition to millions of annual cardiovascular events and the rising costs of healthcare, the epidemics of overweight and obesity highlight the inadequacies of our current strategy. Both ethical and economic considerations implore the need for dramatic change.

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Disclosures

None.

References


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Dariush Mozaffarian, Peter W.F. Wilson and William B. Kannel

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