prediction, ease of reproducible and standardized measurement, relative stability in individuals over time, ability to add to the risk information disclosed by standard measurements such as the components of the Framingham risk score, and most importantly, the demonstration in a large-scale trial (JUPITER) that allocating therapy can reduce cardiovascular events in those deemed ineligible by traditional risk assessment criteria. The addition of information regarding a family history of premature atherosclerosis (a simply obtained indicator of genetic susceptibility), together with the inflammation marker hsCRP, permits correct reclassification of risk in individuals, especially those whose Framingham scores place them at intermediate risk.

Available data do not support the routine use of imaging studies to screen for subclinical disease (e.g., measurement of carotid intima-media thickness, coronary artery calcification, and use of computed tomographic coronary angiograms [CTA]). Inappropriate use of such imaging modalities may promote excessive alarm in asymptomatic individuals and prompt invasive diagnostic and therapeutic procedures of unproven value for both asymptomatic atherosclerosis and incidental findings. Widespread application of such modalities for screening should await proof that targeting therapies based on their application provides clinical benefit.

The 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk recommends the use of newer risk markers if uncertainty persists after assessing quantitative risk using the pooled cohort calculator. The guideline states that family history, hsCRP, coronary artery calcium (CAC) score, or ankle-brachial index (ABI) may then be considered to inform treatment decision making. It discourages carotid intima-media thickness (CIMT) for routine measurement in clinical practice for risk assessment for a first ASCVD event. The guideline panel deemed the contribution to risk assessment for a first ASCVD event using apolipoprotein B (ApoB), chronic kidney disease, albuminuria, or cardiorespiratory fitness as uncertain at present.

Progress in human genetics holds considerable promise for risk prediction and for individualization of cardiovascular therapy. Many early reports identified single-nucleotide polymorphisms (SNPs) in candidate genes as predictors of cardiovascular risk. The validation of such genetic markers of risk and drug responsiveness in multiple populations often proved disappointing. The era of GWAS has led to discovery of sites of genetic variation that reproducibly indicate heightened cardiovascular risk (e.g., chromosome 9p21). The advent of technology that permits relatively rapid and inexpensive exome or whole-genome sequencing promises to identify new therapeutic targets, sharpen risk prediction, and deploy preventive or therapeutic measures in a more personalized manner. Despite this considerable promise, genetic scores for risk prediction have not yet demonstrated consistent improvement over algorithms that use traditional tools.

THE CHALLENGE OF IMPLEMENTATION: CHANGING PHYSICIAN AND PATIENT BEHAVIOR

Despite declining age-adjusted rates of coronary death, cardiovascular mortality worldwide is rising due to aging of the population and due to subsiding of communicable diseases and increased prevalence of risk factors in developing countries. Enormous challenges remain regarding translation of the current evidence base into practice. Physicians must learn how to help individuals adopt a healthy lifestyle in a culturally appropriate manner and to deploy their increasingly powerful pharmacologic tools most economically and effectively. The obstacles to implementation of current evidence-based prevention and treatment of atherosclerosis involve economics, education, physician awareness, and patient adherence to recommended regimens. Future goals in the treatment of atherosclerosis should include more widespread implementation of the current evidence-based guidelines regarding risk factor management and, when appropriate, drug therapy.