The article by Marmo et al\(^1\) provides further information about the use of lifetime as opposed to short-term risk prediction.\(^2\) Previous publications have documented the high lifetime risk of coronary heart disease (CHD) in both men and women.\(^3^,\(^4\)\) Very few women and younger adults, both men and women, had high short-term risk, but many are at high long-term risk. The current article also documents that few in the US population are at both low short-term and long-term risk, 26\%, whereas two thirds of 82\% of those classified as low short-term risk are at high lifetime risk. Furthermore, only 8.4\% of men and 14.3\% of women are at both low lifetime risk and have optimal risk factor levels.\(^1\)

**Editorial**

**Risk Estimation in 2009**

Lewis H. Kuller, MD, DrPH

The high lifetime risk, as reported, is not unexpected. Atherosclerosis is the disease of primary interest.\(^6^,\(^7\)\) It begins in childhood, and the prevalence increases with age. At older ages, the prevalence of atherosclerosis in both the coronary and other arteries is very high, at least in the US population, especially when compared with countries that have low incidence and mortality from CHD. Elevated LDL and apolipoprotein-B (ApoB) are the primary determinants of atherosclerosis and the earlier age in which LDL or ApoB is elevated above a threshold, such as an LDL of \(\leq 70\) mg\% or an ApoB of \(\leq 80\) mg\%, the greater the subsequent extent of atherosclerosis and risk of heart attacks over time.\(^8^--\(^10\)\) The other key risk factors, such as BP, cigarette smoking, and diabetes, contribute to the rate of progression of atherosclerosis given a specific level of LDL cholesterol, ApoB. The risk of CHD becomes greater as the prevalence of atherosclerosis increases, as measured in vivo by extent of coronary calcium.\(^11\) Unfortunately, most individuals in the United States have LDL or ApoB levels above the likely threshold for the prevention of atherosclerosis—126 million with LDL cholesterol \(\geq 100\) mg\%.\(^12\) The higher lifetime risk, as reported in this article, measures the long incubation period for the development and high prevalence of atherosclerosis. Short-term high-risk prediction measures risk for individuals who probably already have extensive atherosclerosis, that is, high 20\% risk in 10 years.\(^2\)

There is, however, not a 1:1 relationship between risk scores and the extent of atherosclerosis because of (1) the usual absence of long-term measures of risk factors in the same individual and substantial within-individual variability of risk factor measurements; (2) the genetic susceptibility for the progression of atherosclerosis, given a specific level of LDL cholesterol or ApoB, that is, host susceptibility; (3) measurement errors for both risk factors and the extent of atherosclerosis; and (4) possible differences in lipoprotein characteristics and other unmeasured risk factors.\(^13\)

The primary clinical use of risk assessment scores, such as the Framingham risk score and the Adult Treatment Panel guidelines, were to define individuals who would be candidates for more aggressive pharmacological versus nonpharmacological therapies, especially lipid-lowering drug therapy. Before the introduction of statin drug therapy, lipid-lowering drugs had relatively modest effects on lowering LDL and the incidence of CHD. These drugs were also expensive, and some had unpleasant side effects. Over time, however, the playing field has dramatically changed. Clinical trials have documented the benefits of statin lipid-lowering drug therapy in both primary and secondary prevention across age and sex groups and even for those with relatively low LDL and ApoB levels.\(^8\)

Among a population with prevalent atherosclerosis, the risk of having a heart attack at any particular time is extremely difficult to measure. The conversion of the atherosclerosis to clinical disease usually requires changes in the atherosclerotic plaque, for example, the vulnerable plaque, hemorrhage, rupture, or erosion of the plaque as well as factors that increase the risk of thrombogenesis and decreased fibrinolysis. The failure to be able to measure the final step, that is, ruptured plaque or thrombosis in population studies of “healthy individuals,” is a major limiting factor for both short- and long-term risk assessment. We can estimate group high or low long-term risk, but within-group individual risk prediction remains elusive. Therefore, we must currently offer preventive therapies to all at high long-term risk to prevent a heart attack. Such an approach is acceptable as long as drugs are safe, effective, and inexpensive. An important research agenda is to identify the “precipitants” of a heart attack, risk factors for thrombogenesis or plaque instability, and development of better pharmacological and possibly nonpharmacological therapies to prevent thrombosis.
Use of noninvasive imaging, such as coronary calcium, provides a further approach to discriminate those who have more atherosclerosis and are at higher risk. Individuals with 0 coronary calcium are at extremely low risk of CHD. Such individuals become rarer with increasing age because the prevalence of atherosclerosis increases over time. Would a combination of noninvasive imaging and long-term risk assessment be superior to identify the at-risk population as compared with each alone and then have a bigger effect on reducing CHD incidence?

CHD is a preventable disease. Individuals who have optimal risk factors have a 5% lifetime risk of a heart attack among men and 8% among women. Could CHD be prevented or reduced to this low lifetime incidence if risk factors could be reduced or actually prevented and low lifetime risk and optimal risk factors increase dramatically above 8% of men and 14% of women? There are 2 options. First, the pharmacological approach to reduction of LDL cholesterol and BP using relatively low-dose therapy applied to most of the population, for example, the polypill, possibly in combination with measures of atherosclerosis to identify more aggressive drug therapies for participants with progressive atherosclerosis even given the polypill therapy. Second, substantially change the American diet to a more plant-based diet with higher intake of polyunsaturated omega-3 and omega-6 fatty acids, and reduce sodium and calories to reduce prevalence of obesity. Increased physical activity and improved cardiovascular fitness may both blunt the obesity epidemic and decrease cardiovascular disease risk.

Individualized nonpharmacological therapy without changing the food processing in a common source epidemic, such as atherosclerosis, is unlikely to be successful. Therefore, a major modification of food processing and distribution and consumer education and possibly regulation would probably have the biggest effect but remains extremely difficult to implement.

We could hope for a pill that will prevent the development of the final thrombosis or ruptured plaque. Such an approach is unlikely to be of substantial benefit alone in reducing the risk of CHD unless the extent of atherosclerotic disease is also substantially reduced by the pharmacological and nonpharmacological approaches.

We have come full circle from the recognition that CHD is an example of a common source epidemic to try and classify individuals arbitrarily into high, intermediate, and low short-term risk to finally recognizing the importance of long-term risk of CHD and the need to treat CHD as a common source epidemic. We hope not to spend the next 20 years developing new risk assessment tools and a never-ending list of “risk factors.”

Disclosures

None.

References


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