The Preventive Potential of Common, Easily Measured Risk Factors for Cardiovascular Disease
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In the 1990s mortality rates for cardiovascular disease (CVD)⁴ were declining in developed countries where the risk factors for acute myocardial infarction (AMI) had been studied. However, CVD was increasing in developing countries and more than 80% of global CVD was predicted to occur by 2020 in low- and middle-income countries, which would be challenged with improving their existing healthcare systems and simultaneously coping with an epidemic of CVD, previously not a healthcare problem for them. At that time known risk factors accounted for only 50% of CVD, implying a need to find new, probably more expensive, risk factors.

Prevention first requires establishing appropriate and cost-effective preventive measures. Could risk factors derived mainly from North American and European males be applicable to other populations and to females? For example, from 1990 to the early 2000s it was thought that lipids were not associated with coronary heart disease in South Asians and blood pressure increases might be more important in Chinese people.

The INTERHEART study design needed large numbers to address risk factors in different ethnic groups, across different regions of the world, to establish each factor’s population attributable risk (PAR) for AMI. The most practical approach to obtain the answers rapidly and affordably was a standardized case control study with many hundreds or a thousand or more AMI events from each region of the world, where most known risk factors and a few emerging risk factors were measured. The alternative cohort study was not feasible, requiring 20–30 times more participants and 5–10 years follow-up and entailing much higher costs. INTERHEART was conducted in 52 countries with 15,152 cases and 14,820 controls enrolled in 4 years from every inhabited continent.

Abnormal lipids; smoking; hypertension; diabetes; abdominal obesity; psychosocial factors; consumption of fruits, vegetables, and alcohol; and regular physical activity accounted for >90% of the risk of a first AMI. From a clinical chemistry perspective, the apolipoprotein B100/apolipoprotein A1 ratio had the highest PAR (54%), and the LDL cholesterol/HDL cholesterol PAR was only 37%, a finding that has contributed to clarifying the best laboratory marker to predict CVD risk (1).

The INTERHEART contribution to public health has been that these easily measured and modifiable risk factors account for most of the risk of AMI, with smoking and lipids together accounting for 70% of the risk. The impact of the 9 factors was global and their effect was consistent in men and women, in different ethnic groups and in different geographic regions, providing a basis for a worldwide strategy for the prevention of CVD, particularly in developing countries and non-white populations. It stimulated the investigators to study the importance of psychosocial factors and socioeconomic status and to apply the INTERHEART understanding and experience to the global investigation of risk factors for stroke, with similar results (2).

Although INTERHEART established many of the risk factors that differentiate risk, what produces increased levels of these cardiovascular risk factors within a country, with different relevance across various segments of its population, was not well understood, and neither were the factors affecting the different risks between countries. There was clearly a complex relationship of societal influences on human lifestyle behavior, cardiovascular risk factors, and the global increase in noncommunicable diseases. These lessons from INTERHEART and other studies are now being applied in the PURE (Prospective Urban Rural Epidemiology) study in 25 low-, middle-, and high-income countries around the world, with 170,000 participants (target of >200,000) currently enrolled. After important risk factors are established, the success of any pre-
ventive strategy depends on understanding what causes these risk indicators to be present, for example, what influences changes in lipids and what influences the individual and combined impacts of all the factors on health in different countries.

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