## An ounce of prevention

The current economic crisis is colliding with healthcare reform in the US and many areas around the world. As debates about the reasons for and solutions to the rising tide of healthcare costs escalate, cardiovascular specialists must focus on prevention and reconsider our ideas of how to go about it.

Disease prevention is generally thought to be expensive and, with the exception of vaccination for communicable diseases, planned prevention strategies have not had a lot to show for themselves. However, major cardiovascular disease accounts for a 7-year reduction of life expectancy-more than any other single cause-and, with an estimated direct and indirect annual US price tag of almost $\$ 500$ billion, there is room for effective prevention. Furthermore, cardiovascular disease is different from other major conditions that reduce life expectancy. In most conditions a highly effective treatment can negate the impact on life expectancy without the need for prevention. Given the nature of first cardiovascular events, however, cardiologists cannot postpone action until after events occur if we want to materially reduce the impact of cardiovascular disease on life expectancy.

High-risk or vulnerable plaques are responsible for most major cardiovascular events. Our prevention strategies currently relate to finding and managing risk factors for the development of these plaques; however, we have three theoretical opportunities for recognition of those at risk—risk factor profile, burden of atherosclerosis, and presence of high-risk plaque(s).

Over the past few decades risk factors such as obesity, diabetes, and sedentary lifestyles have increased, and the incidence of predominantly medication-controlled risk factors (hypertension and lipid disorders) have only gradually decreased. Moreover, three of the key risk fac-tors-age, gender and family history-cannot be modified, so although risk factors can be a key to identifying individuals with elevated risk, only lifestyle changes and pharmacological means can provide a material solution for such people.

The financial burden of risk factors is a heavy one. Indeed, it has been estimated that every pound an adult is overweight adds $\$ 19.39$ to annual US healthcare costs. Given the number of overweight and obese adults in the US, this adds up to more than $\$ 127$ billion per year. Again, these numbers reveal the magnitude of the opportunity that new paradigms in prevention can help realize.

The economic opportunity associated with prevention has also been illustrated by an examination by Humana Inc. of the healthcare costs for at-risk asymptomatic individuals with no history of heart disease; some of these
individuals went on to have heart attacks or strokes and others did not. The annual healthcare costs for individuals who did not have events started at $\$ 3,500$ and rose to $\$ 5,000$ over a 3 -year period. For people who experienced an event, their starting annual costs were similar, but increased to over $\$ 20,000$ as they experienced myocardial infarction or stroke.

Primary prevention is almost exclusively focused on recognition and management of risk factors, yet the unaddressed problem is that most people destined for a myocardial infarction or a stroke are unaware of their risk. Indeed, most heart attacks and strokes occur in individuals who would be classified as being at low or intermediate risk by the traditional risk-scoring algorithms, such as the Framingham Risk Score-their traditional risk factor levels are not high enough to signal the need for treatment. Focusing only on those with the highest risk has a small impact on overall outcomes; however, focusing on the proportion of the population who experience the majority of events would require us to intervene with nearly the entire population. This is the risk factor dilemma.
If risk factor reduction were easy and affordable, a workable strategy would be to reduce risk factors in the general population. Indeed, at either end of the prevention spectrum - treating everyone or finding those who would become this year's heart attack or stroke victimeconomic viability and potential solutions are available. These solutions are essential if we want to reduce the financial burden and improve life expectancy.

At one end of the spectrum lies public policy addressing tobacco, salt reduction and cooking oil, as well as concepts such as the polypill (for example, the combination of low-dose aspirin, an angiotensin-converting enzyme inhibitor and a statin). This latter concept relies on our acceptance that events occur in males and females above a gender-specific cut-off age and that simple pharmacological intervention might be necessary for (nearly) all. This strategy can be cost-effective-a low level of efficacy is all it takes for a safe medication to become costeffective in the long term-and is, by definition, easy to implement. The safety profile of the preventative medication and the low cost of distribution also support such a strategy. In the US alone, over 85 million people would be eligible for this approach to disease prevention.
At the other end of the spectrum lies the need to be able to reliably and simply identify people before their first heart attack or stroke. Reliable identification of at-risk people before their first heart attack or stroke is dependent on the performance and cost of the diagnostic ...cardiovascular specialists must focus on prevention and reconsider our ideas of how to go about it 77

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## Acknowledgments <br> The economic data

 included in this Editorial was provided by the health benefits company Humana Inc.Competing interests The author declares an association with the following company: B. G. Medical. See the article online for full details of the relationship.
assay. The ideal test would, with a high degree of certainty and simplicity, identify individuals who are at risk of experiencing a major event in the short term (5-10 years) and allow us to administer appropriate treatment to prevent the potential event(s). If used by the same 85 million people in the US who are eligible for a polypill, this approach would identify approximately 2 million people at very high short-term risk for heart attack or stroke and, therefore, need to be treated. Identification of people at risk could involve identification of risk factors or identification of subclinical atherosclerosis (for example, by simple noninvasive imaging). Indeed, new methods for identification (for example, evolving proteomics from blood sampling) and treatment of subclinical atherosclerosis could potentially surpass conventional risk factor management in terms of overall impact on morbidity, mortality and healthcare costs. Success of this strategy, however, relies not only on our ability to establish new paradigms for the detection, screening and treatment of subclinical atherosclerosis, but also to dismantle old ones.

As stated above, with direct and indirect costs of cardiovascular disease being estimated as hundreds of billions of dollars per year in the US, there is room for effective prevention. Even if an effective blood or imaging test costs $\$ 100$ and all 85 million at-risk individuals complied, the expenditure would amount to no more than $\$ 8.5$ billion. Assuming a treatment cost of $\$ 2,000$ per year for the 2 million people identified, the cost would increase by $\$ 4$ billion. Even if they remained on therapy for the rest of their lives to prevent an event, the combined cost is well below the current price tag of managing individuals after events have occurred.

One of the most important economic opportunities in healthcare is prevention of major disease. It doesn't take an economist to recognize that new paradigms in effective primary prevention are well within the boundaries of the health system's current framework of diagnostic tests and treatments. Moreover, such paradigms are critical to solving the Da Vinci code of healthcare reform. The answer to this problem, however, should not be in the hands of policy makers or economists, but in the hands of scientists. Scientific advances over the past few years have pointed us in the right direction for better diagnosis and treatment. Vulnerable plaques result from a dynamic multistep disease process with several suitable points for effective intervention, and the proximity of the plaque to the vessel wall makes it highly plausible that reliable blood tests and imaging will evolve as valuable tools in the near future.
So, although the emerging enthusiasm for primary prevention of cardiovascular disease is encouraging, studies should be designed and interpreted with their broad context-including health economics-in mind. I estimate the average age of the reader of this article to be 45 and, therefore, it is in our own best interests that this problem be addressed as soon and as aggressively as possible. If the scientific community and industry came together to tackle atherothrombosis in a way analogous to the massive efforts around HIV and AIDS in the 1980s and 1990s, I am confident we can develop effective diagnostic tests and therapeutic strategies that will allow an economic return unmatched by any previous policy decision.
doi:10.1038/nrcardio.2009.153

