# Reducing cardiovascular risk: too little, too late, too short-term

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Vascular diseases in general, and cardiovascular disease in particular, are diseases of mass destruction, killing more people in the Western world (and increasingly in the developing world) than world wars. Each year, coronary heart disease kills over half a million Americans and over 100 000 British citizens each year, often prematurely (WHO online).

A combination of migration, epidemiological, and intervention studies confirm that lifestyle affects the onset and progression of disease. Most of the excess risk of coronary disease, at least in Western societies, is attributable to well recognized major independent risk factors (cigarette smoking, hypertension, elevated total and low-density lipoprotein (LDL) cholesterol, low high-density lipoprotein (HDL), diabetes mellitus, and advancing age). Epidemiological studies have shown a continuum of risk for increasing levels of blood pressure, total cholesterol, LDL, and smoking (Wilson 1998). These are aggravated by a variety of contributory predisposing factors (obesity and abdominal obesity, physical inactivity, family history of premature coronary disease, and ethnic characteristics), psychosocial factors, and conditional risk factors (elevated triglycerides, small LDL particles, prothrombotic factors such as fibrinogen, insulin resistance, and abnormal levels of lipoprotein(a) and homocysteine).

The UK heads most league tables for premature mortality and morbidity from vascular disease. While crude statistics adequately describe populations, illness affects individuals, and the principal objective of preventive medicine is to minimize the risk of avoidable vascular events in individuals at varying degrees of susceptibility.

## Measuring risk

Risk scoring systems have been developed from long-term observational studies such as the Framingham (USA) study, which followed first one and now two generations of middle class white families (NHLBI online). Scoring systems acknowledge the multifactorial causation of vascular disease, sex differences in disease prevalence, and increased risk due to the aging process. A variety of tables, charts, and software packages are available, differing predominantly in their usability and graphic presentation, but all provide an *estimate* of global cardiovascular risk (and with some calculators, stroke risk).

Risk calculators are designed for primary prevention only – once vascular disease has become clinically apparent, whether in cardiovascular, cerebrovascular, or peripheral vessels, the likelihood of recurrent disease is very high. Formal risk assessment is inappropriate, and all potentially reversible risk factors must be addressed to minimize disease progression.

Calculators provide an estimate of "absolute" risk, which is the probability of developing disease over a finite time period, usually ten years. Some scoring systems allow an estimate of "relative" risk; that is, the ability to differentiate individuals at "high" risk from those at some intermediate or "low" risk.

## Problems with risk calculators

Risk scoring systems are imperfect tools which have been derived from a population comprising thousands of individuals. Although scores indicate the potential extent of risk, clinicians (and patients) must be aware that the future outcome of a specific individual remains uncertain. The risk estimate should be considered an "average" because biological variability, inevitable in any population, can generate a large spread of risk around the average. In practical terms, this means that the estimate of risk for a group will be correct, but the estimate for an individual could be widely astray. It is entirely feasible that two people with the same risk score may experience different outcomes.

The ease with which a risk score can be derived is not matched by the certainty of outcome; the score provides no more than a "best estimate" of an individual's risk status and fate. More than half of all coronary deaths and most cases of myocardial infarction occur in those whose risk prediction score would be considered to have a "low" or "moderate" risk of a coronary event, reflecting the Gaussian distribution of risk factor profiles in a given population. Those involved in risk assessment need to be aware that a person with a "low" risk may develop vascular disease while someone at "high" risk may avoid it.

The databases from which the scoring systems were developed included information on the major *independent*

risk factors but did not take into account *predisposing* and *conditional* risk factors. For example, evaluation of some conditional risks such as LDL particles and serum lipoproteins were not available to the Framingham monitors (abnormal levels of these will increase the estimated risk). The Framingham population were white and so an adjustment needs to be made for individuals of other ethnic backgrounds such as South Asians who have a 40% greater risk of coronary disease. Consequently, in many cases, the risk estimate should be considered to be *minimum* level of risk.

It is tempting to assume (but there is no evidence to support the concept) that reducing a risk factor by a given amount will reduce overall risk to the same extent as an increase in the same risk factor increases total risk. Even if an individual's lifestyle changes are rewarded with a marked reduction in estimated risk, vascular risk is never zero and so there can be no guarantee that an untoward vascular event will not occur.

At the start of the Framingham study, few individuals had diabetes mellitus. The prevalence of diabetes is high and increasing in many populations, and this can have a marked influence on absolute risk.

## The greatest risk of all

Reducing *reversible* factors such as cholesterol and blood pressure can reduce risk, but one factor dominates the risk equation: with advancing age, risk inevitably increases. For example, a non-smoking male aged 35–44 with a ratio of total cholesterol to HDL of 6 and a systolic blood pressure of 150 has over the next ten years a 15% risk of a coronary event; at 45–64, bearing the same blood pressure and cholesterol (though both may increase with age), his risk is between 15% and 30%, and by the time he reaches 65, he has a greater than 30% risk. This supports the concept that risk factor management needs to be instituted early and aggressively.

## What is high risk?

The National Service Framework (NSF) for Coronary Heart Disease defines "high risk" of developing coronary disease in the subsequent ten years as greater than 30% (Department of Health 2000). The proportion of the UK male population with this degree of risk is about 3%. A further 16% have a risk of 20% or more, and over half the adult male population has a risk greater than 15%. For women, the overall risk is less than half that of males.

If clinicians concentrate, as the NSF recommends, on identifying and treating what Rose (1992, p 31) described as "the deviant minority at high risk", individuals may well benefit, but there will be negligible impact on national mortality and morbidity figures because intervention is being offered to such a small proportion of the "at-risk" population. Achieving a significant reduction in avoidable vascular mortality and morbidity requires a shift in the population mean risk.

## Is the level of "high risk" set too high?

Although fewer coronary events occur in populations with low levels of risk factors, coronary events occur at all levels of risk – no level of risk can be considered "safe".

Government may set the risk threshold for political reasons and may also dictate to what extent the state is prepared to protect the individual. Speed limits and central crash barriers were introduced as knee-jerk reactions to motorway accidents in poor visibility. In real terms, most people in a lifetime of driving are at low risk of encountering such an accident (unlike vascular disease), so the concept of risk and risk reduction seems to be poorly understood.

The individual, however, must make a decision about what degree of risk is personally acceptable and when (and what) interventions are necessary.

Adoption of a 30% ten-year risk to trigger primary prevention denies the majority of the UK population the opportunity to prevent, or at least delay, a first vascular event. Targeting those at high risk means that intervention is delayed unnecessarily in those at more modest levels of risk, exposing the vascular system to years of atherogenic challenge from diabetes, hypertension, hypercholesterolemia, and progressively increasing the burden of plaque formation.

In this respect, it is illogical to delay intervention until some arbitrary threshold of risk is reached. Even a modest risk will, with time, reach levels which currently warrant intervention, but long after atheromatous plaque has developed throughout the arterial tree.

The risk factor burden of people in their twenties and thirties needs to be reduced, as atherogenesis begins early and is a lifelong hazard. For them, a ten-year perspective is short term.

## The population approach to risk

For years, clinicians were encouraged to treat a single risk factor – hypertension. Addressing multiple risk factors

increases the likelihood of benefit as the absolute risk is higher, making intervention, including drug treatment, more effective and more cost-effective.

When risk is common to many people, as is vascular risk, a population-wide intervention strategy is more appropriate. If a significant impact on premature mortality and morbidity is to be achieved, it is essential to expand the target population to include lower levels of risk. Because long-term drug treatment can only be justified in high-risk individuals, a population strategy must address lifestyle changes to reduce risk.

In prevention terms, population strategies are more likely to be successful than targeted policies. In reality, we are practicing medical communism, whereby preventing an adverse outcome requires many people to reduce their individual risk – this is the "prevention paradox". This principle applies as much to common infectious disease (like whooping cough or measles) and chronic degenerative diseases (such as stroke and heart attack) as it does to public health measures including legal enforcement of speed limits, use of seatbelts, wearing of motorcycle helmets, and fluoridation.

## Which risk – relative or absolute?

Relative and absolute risk can be determined from several risk calculators. Absolute risk lends itself to the identification of individuals who should be advised on risk factor reduction. Absolute risk, however, increases with age, despite low cholesterol, low blood pressure, and a no-smoking habit. This has two implications. First, an increasing proportion of the population will reach the high-risk threshold that currently warrants intervention (the 30% risk). Second, more of those at modest risk will become high risk. In both cases, applying the present 30% rule delays intervention and permits years of overexposure to the atherogenic process.

Relative risk, which decreases with age, can also inform clinicians. Younger individuals with a high *relative* risk (compared with their peers) face the additional challenge of increased *absolute* risk with aging; they should be targeted for long-term intervention to reduce risk. Older patients are at high risk because of age; under present guidance, all will be offered intervention, but those with a high relative risk (compared with their peers) may be more worthy of aggressive risk factor reduction in the short term.

The current high-risk strategy based on a high absolute risk alone misses opportunities to intervene at an early stage in risk, and atheroma, development.

## Primary prevention: time for a reappraisal

Guidelines on levels of risk at which primary prevention should be initiated are inappropriately high. A strategy that targets only those with high risk ignores clinical evidence that absolute risk increases with age, the overriding factor in risk calculation. In practice, this means that, despite more becoming appropriate for intervention with advancing age, delayed intervention allows vascular plaque load to increase unabated. A high-risk strategy applies to too few, too late to have a major impact.

If primary prevention is to be effective, and to reduce avoidable mortality and morbidity, a population strategy should be introduced. Not only does the total risk factor burden of the nation need to be addressed, which is a major challenge for public health, but also younger patients with excess relative risk should be considered for long-term lifestyle intervention, with medication if essential. Finally, the emphasis on a ten-year horizon instead of a ten-year risk score, the perspective appropriate for younger individuals, should be twenty years, or even longer.

## References

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