

## **Factors that Affect Cardiovascular Health: A Review**

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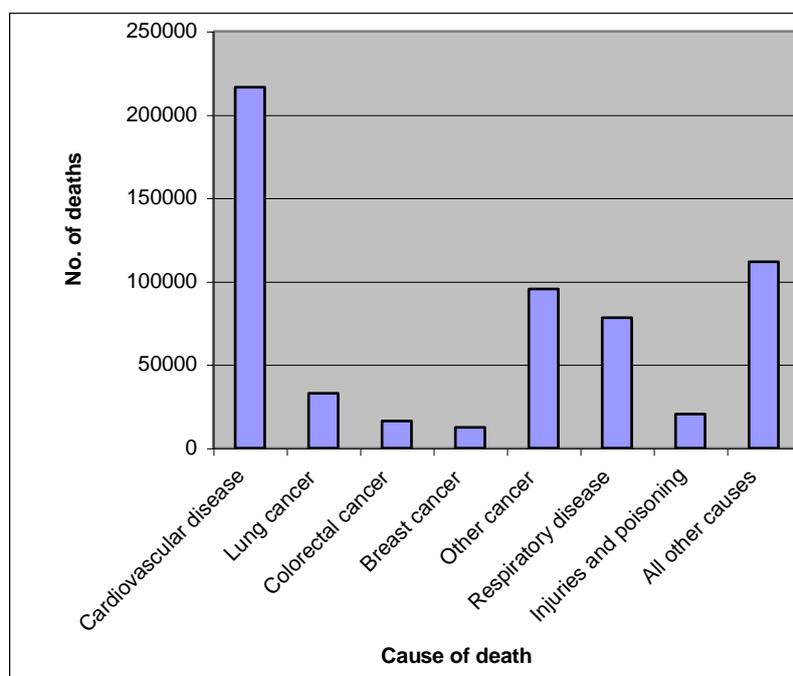
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**Summary:** Cardiovascular disease is a major public health problem in terms of both high morbidity and mortality rates and large economic costs. Cardiovascular health and risk of disease are determined by a wide range of genetic and environmental factors. This review focuses on the extent to which heredity, physical activity, diet, and psychological factors (including stress) are known to contribute to cardiovascular health or disease. A predisposition for cardiovascular disease can be inherited, but genetic counselling allows the identification of those who are most at risk and an individualised plan to include appropriate lifestyle changes can then be formulated. It is well established that increasing amounts of physical activity can enhance cardiovascular health and reduce the risk of disease, but knowledge of specific aspects of exercise (such as optimal intensity and mode) is limited. Dietary interventions show that reductions in low-density lipoproteins (LDLs), and increases in high-density lipoproteins (HDLs) and certain antioxidants and vitamins may reduce cardiovascular disease risk factors. The long-term effects of dietary salt are more controversial. Psychological factors are contributory, rather than major, determinants of cardiovascular health, but there is evidence that lack of social support, stress and other negative states can increase the risk of disease.

**Key words:** Cardiovascular disease, risk factors, heritability, physical activity, diet, stress.

## Introduction

Cardiovascular disease includes several diseases of the heart and circulatory system, the most common being arteriosclerosis, coronary heart disease, stroke and hypertension. Cardiovascular disease is a major health problem and remains the leading cause of death in many industrialised countries (British Heart Foundation 2006). In comparison with other common causes of mortality in the United Kingdom, cardiovascular disease accounts for an extremely high number of deaths (as shown in Figure 1). In 2004, more than 216,000 people in the UK died as a result of cardiovascular disease, and almost 60,000 of these deaths were premature, i.e. occurring before the age of 75 (British Heart Foundation 2006). Furthermore, there are great economic costs associated with this disease. Cardiovascular disease was estimated to have cost the UK just under £26 billion in total in 2003; the costs of coronary heart disease make up almost a third of this amount (see Table 1).



**Figure 1: Total deaths by cause in the United Kingdom in 2004**

(adapted from British Heart Foundation Health Promotion Research Group 2006, [www.heartstats.org](http://www.heartstats.org))

**Table 1: Costs of cardiovascular disease (CVD) and coronary heart disease (CHD) in 2003, United Kingdom**  
(extracted from British Heart Foundation 2005, www.heartstats.org)

	CVD		CHD	
	£ million	% of total	£ million	% of total
Health care costs	14,732	57	3,527	45
Production losses due to mortality	3,677	14	2,173	27
Production losses due to morbidity	2,556	10	961	12
Informal care	4,835	19	1,249	16
Total	25,799	100	7,910	100

It is therefore clear that maintaining cardiovascular health and preventing disease should be a chief governmental priority. A number of factors that can affect cardiovascular health and disease have been identified and are shown in Table 2. Importantly, the majority of these factors can be modified by lifestyle changes (Powers & Dodd 2003). This review will analyse in more depth four main factors that contribute to cardiovascular health or disease: heredity, physical activity, diet and psychological factors.

**Table 2: Factors that affect cardiovascular health and disease**

Factor	Example of study that has associated factor with cardiovascular health or disease	Is the factor modifiable by behavioural changes?
Heredity	Knuiman <i>et al.</i> (1996)	No
Physical activity (amount of exercise)	Paffenbarger <i>et al.</i> (1993)	Yes
Diet	Estruch <i>et al.</i> (2006)	Yes
Psychological factors (including stress)	Greenlund <i>et al.</i> (1995)	Yes
Age	Wang <i>et al.</i> (2006)	No
Gender	Perusse, Moll, and Sing (1991)	No
Race/ethnicity	Freedman <i>et al.</i> (2005)	No
Physical fitness (maximal exercise capacity)	Blair <i>et al.</i> (1989)	Yes
Hypertension	Wang <i>et al.</i> (2006)	To some extent
Heart rate	Kristal-Boneh <i>et al.</i> (2000)	To some extent
Smoking	Auerbach and Garfinkel (1980)	Yes
Alcohol	Marmot <i>et al.</i> (1994)	Yes
Obesity	Zhao <i>et al.</i> (2002)	Yes
Diabetes	Govind <i>et al.</i> (2005)	To some extent
Infection ( <i>Helicobacter pylori</i> )	Sung <i>et al.</i> (2005)	To some extent
Air pollution	Hosseinpour <i>et al.</i> (2005)	To some extent
Socio-economic status	Manios <i>et al.</i> (2004)	To some extent

## Heredity

Various studies have established that a family history of cardiovascular disease is associated with an increased risk. Evidence suggests that this familial risk is linked to factors such as blood pressure, heart rate, blood cholesterol levels, obesity and diabetes (Powers & Dodd 2003; Turnpenny & Ellard 2005). Lusi (2003) points out that when such factors are taken into account, at least hundreds of genes can play a role in determining cardiovascular health and disease.

The familial occurrence of cardiovascular disease and associated risk factors has long been a focus of research. An early study by Barret-Connor and Khaw (1984) revealed that family history of heart attack was an independent predictor of death caused by cardiovascular disease. In a study of 1319 nuclear families, Knuiman *et al.* (1996) estimated the heritability, i.e. the proportion of phenotypic variance attributable to additive genetic variance, of several cardiovascular risk factors (as shown in Table 3). The researchers concluded that there are significant familial correlations of cardiovascular risk factors and that genetics are an important component of this, but assortative mating in spouses and shared environmental factors (in offspring and siblings) also play a role.

**Table 3: Estimated heritabilities of various cardiovascular risk factors**  
(adapted from Knuiman *et al.* 1996: p192)

<b>Risk factor</b>	<b>Estimated heritability</b>
Systolic blood pressure	27 %
Diastolic blood pressure	27 %
Body mass index	52 %
Triceps fatfold	23 %
Serum cholesterol	37 %

Heart rate (HR) and heart rate variability (HRV) also appear to have a substantial genetic component. The Framingham Heart Study (Singh *et al.* 1999) found that correlations in HR and HRV were significantly greater between siblings compared with spouses, and it was calculated that 13-23% of the variance in HR and HRV could be explained by genetic factors. However, there is some debate over whether heart rate is a reliable measure of cardiovascular health; whereas some researchers (such as Palatini 2006) believe that heart rate is an independent predictor of cardiovascular mortality, others (e.g. Benetos 2000) state that heart rate is insignificant in comparison to more important risk factors.

Recent studies have attempted to identify specific genes that contribute to cardiovascular health and disease. An apparent breakthrough came in 2003 when Wang *et al.* claimed to have discovered the first autosomal dominant gene for coronary heart disease and myocardial infarction at the *MEF2A* locus on chromosome 15q26. This conclusion was reached by analysing the genomes of only one family, however, and more recent evidence has suggested that mutations at the *MEF2A* locus are a much less common cause of coronary heart disease than originally anticipated (Weng *et al.* 2005).

A number of genomewide linkage scans have identified additional susceptibility loci for cardiovascular disease. Francke *et al.* (2001) found that chromosome 16p13 was implicated in coronary heart disease in a sample of Indo-Mauritians. Hauser *et al.* (2004) identified a region on chromosome 3q13 that was

linked to early-onset coronary heart disease. In addition, The British Heart Foundation Family Heart Study (Samani *et al.* 2005) revealed a region on chromosome 2 that seems to be associated with premature coronary heart disease and myocardial infarction.

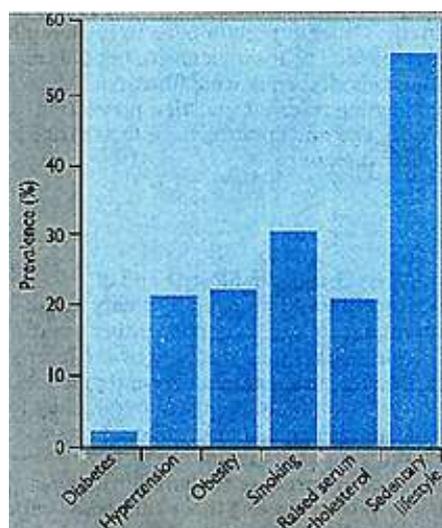
Blood pressure is considered to be a well-established measure of cardiovascular health (Kelley, Kelley & Tran, 2001) and is determined by both genetic and environmental factors (Turnpenny & Ellard 2005). Hypertension, or high blood pressure, is unique in that it can simultaneously be regarded as a cardiovascular disease in itself and a risk factor (Powers & Dodd 2003). Various studies have found positive associations between hypertension and risk of developing coronary heart disease (e.g. Wang *et al.* 2006). Identification of the genes involved in hypertension is an extremely well researched area. Recent research by Zhu *et al.* (2005) has found evidence for loci of major importance in influencing hypertension on chromosomes 6q24 and 21q21.

Despite the identification of large numbers of genetic loci that are potentially involved in the determination of cardiovascular health and disease, the results are inconsistent. One of the main criticisms of genetic association studies is failure to replicate findings; Hirschorn *et al.* (2002, as cited in Sturm 2004) showed that only 3.6 % of associations between common gene variants and disease have been consistently replicated.

Evidence suggests that cardiovascular disease is a multifactorial disorder, i.e. cardiovascular health is determined by multiple genetic and environmental factors (Powers & Dodd 2003; Turnpenny & Ellard 2005). Although several susceptibility loci associated with cardiovascular disease and its risk factors have been found, we do not currently have a complete understanding of the complex genetics involved. However, Sturm (2004) argues that the primary goal of cardiovascular genetic research can now be achieved – to reduce morbidity and mortality due to cardiovascular disease by identifying people who are most at risk through genetic counselling. As well as possible drug therapy, a key component of this counselling should be an individualised plan to include lifestyle changes to improve cardiovascular health and reduce the risk of disease. This review will now focus on the role of lifestyle factors in cardiovascular health and disease.

### Physical Activity

Lack of physical activity has been recognised as a major risk factor for cardiovascular disease since 1992 (Powers & Dodd 2003). There is indisputable evidence to show that regular exercise is effective for improving cardiovascular health and reducing disease. This evidence comes from both laboratory studies of monkeys (e.g. Williams *et al.* 2003) and natural studies of both leisure and occupational activity in humans (e.g. Noda *et al.* 2005; Hu *et al.* 2005). In spite of this evidence, many people still do not engage in frequent physical activity. Relative to other risk factors for cardiovascular disease, a sedentary lifestyle is of high prevalence (as illustrated in Figure 2).



**Figure 2: The prevalence of some important risk factors for cardiovascular disease (a sedentary lifestyle means physical activity fewer than three times per week or less than 20 minutes per session)**  
(extracted from Fentem 1994)

As previously stated, blood pressure is generally considered a reliable measure of cardiovascular health. The benefits of exercise for lowering blood pressure have been widely investigated. For example, Whelton *et al.* (2002) conducted a meta-analysis of randomised, controlled trials and found that aerobic exercise was associated with significant reductions in resting systolic and diastolic blood pressure in both hypertensive and normotensive individuals. Another meta-analysis revealed that walking exercise programs in adults resulted in reductions in blood pressure of approximately 2 % (Kelley, Kelley, & Tran, 2001). However, such reductions are not found in all people; it seems that this may be due to age-related differences in the effects of exercise on blood pressure. Wei, Li and Ragland (1987) found evidence for differential effects of exercise on resting blood pressure in adult and aged rats, and a meta-analysis by Kelly, Kelley and Tran (2003) showed that exercise intervention did not lead to significant reductions of resting blood pressure in children or adolescents.

The physiological mechanisms involved in the long-term cardiovascular benefits of exercise are not completely clear at this time and should be the focus of additional research. Some potential explanations are structural adaptations including hypertrophy of the heart and improvements in vascular number and structure, and neurohumoral adaptations including improved insulin sensitivity and alterations in vasodilators and vasoconstrictors (Pescatello *et al.* 2004).

Despite public guidelines being in place for the recommended quantity of exercise (e.g. Bouchard, Shephard & Stephens, 1993), the methodology used by many studies has been criticised and several deficiencies in our knowledge concerning physical activity and cardiovascular health still exist. Houde and Melillo (2002) propose that sample sizes have generally been too small, and that interventions, measures of physical activity and outcomes vary widely between studies. Kelley, Kelley and Tran (2001), reviewing a number of studies, also argue that better control of extraneous variables that can affect cardiovascular health is needed. Furthermore, the effects of exercise on cardiovascular health have principally been determined in a

limited number of populations; women, children and certain ethnic groups appear to be less well researched.

Future studies should focus not on the benefits to cardiovascular health of exercise in general, but on specific aspects of exercise – mode or type, frequency, duration and intensity (Pescatello *et al.* 2004). To date, research is increasing in these areas. I am currently conducting an investigation into whether cardiovascular health, determined by resting blood pressure and heart rate, is affected by exercise type (golf vs. tennis) and impact (low or high). I also aim to establish whether age- or gender-related differences exist in any effects observed.

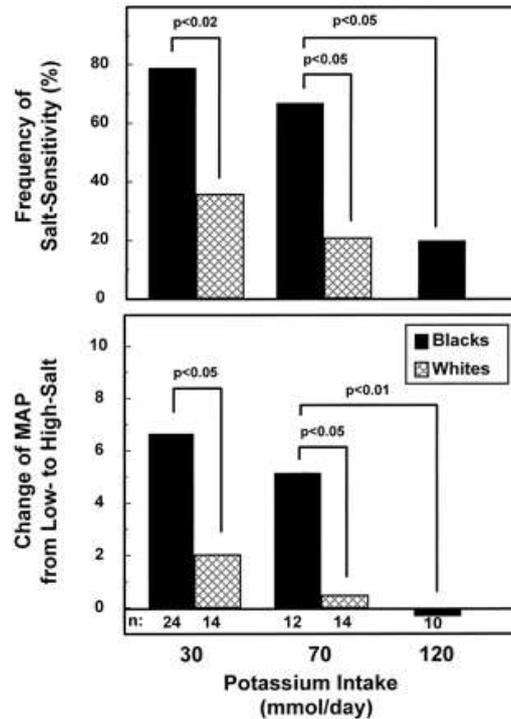
A similar study of exercise type by Cox (2006) compared the effects of walking and swimming and observed an unexpected significant increase in the systolic blood pressure of previously sedentary female swimmers, relative to walkers, after six months. Additional recent studies have focused on different aspects of exercise and cardiovascular health; for example Manson *et al.* (1999), in a longitudinal study of women, found that brisk walking and vigorous exercise were associated with similar reductions in coronary heart disease incidence.

## Diet

The most studied diet-related factors that can influence cardiovascular health are saturated fatty acids and cholesterol, and dietary salt. More recently, however, the effects of a wider variety of nutrients and diets have also been considered.

Cholesterol can be either consumed in the diet or synthesised in the body. A high blood cholesterol level (hypercholesterolemia) is a primary risk factor for cardiovascular disease (Nicolosi *et al.* 2001). Diets low in saturated fats and cholesterol, and high in unsaturated fats are recommended for both prevention and treatment of cardiovascular disease (Powers & Dodd 2003). Cholesterol can combine with protein in the liver to form either low-density lipoproteins (LDLs) or high-density lipoproteins (HDLs). Research has shown that high blood LDL levels are associated with an increased risk of coronary heart disease and stroke, whereas high HDL levels are associated with a reduced risk (e.g. Psaty *et al.* 2004). Nicolosi *et al.* (2001) have summarised several dietary interventions that have been shown to lower LDLs but do not affect HDLs, including soluble fibres, soy protein, lecithin, plant sterols and rice bran oil. According to National Institute of Health guidelines, the optimal total blood cholesterol concentration is less than 200 mg per decilitre and the optimal LDL concentration is less than 100 mg/dl (Powers & Dodd 2003).

Dietary salt has been studied mainly in relation to its short-term and long-term effects on blood pressure. There is substantial evidence that a high salt intake can contribute to hypertension (Karppanen & Mervaala 2006); this increased blood pressure is principally due to increases in blood volume. However, the link between salt intake and cardiovascular morbidity and mortality seems to be less clear-cut, and there appear to be individual differences in the effects of salt in the diet. Morris *et al.* (1999) found that the extent to which people are salt-sensitive (i.e. show an increase in mean arterial blood pressure of 3 mmHg or more after high salt intake) varies according to race and dietary potassium levels. These researchers also found that increasing potassium intake could eliminate the rise in blood pressure in salt-sensitive individuals (as shown in Figure 3).



**Figure 3: Reductions in mean arterial blood pressure (MAP) and salt sensitivity with increased dietary potassium intake in normotensive black men and white men**  
(extracted from Morris *et al.* 1999: p20)

Alderman (2004), following a review of a number of studies on the health effects of dietary salt, argued that results are inconsistent, and that there is currently insufficient evidence to suggest that restricting salt intake is of any benefit to the cardiovascular health of either normotensive or hypertensive persons.

It now appears that a wider range of nutrients can influence cardiovascular health independent of any effects on cholesterol levels. A diet rich in polyphenols (antioxidants found in fruits and vegetables), isoflavones (from soy protein), folic acid and vitamins B<sub>6</sub> and B<sub>12</sub> may reduce the risk of cardiovascular disease (Nicolosi *et al.* 2001). However, the mechanisms by which such nutrients act to improve cardiovascular health are unclear and not all studies find beneficial effects. For example, a controlled intervention study by Broekmans *et al.* (2001) found no effects on serum lipids, blood pressure or other haemostatic variables in participants with increased fruit and vegetable intake. Estruch *et al.* (2006), on the other hand, recently found that a Mediterranean diet, high in either nuts or olive oil, reduced cardiovascular risk factors (including blood pressure, lipid profile and inflammatory molecules) in comparison to a low-fat diet.

A limitation of the two previous studies is that only short-term outcomes were assessed. There is a need for more investigations into the long-term effects on cardiovascular health and mechanisms of action, including possible interactions, of different dietary factors (Nicolosi *et al.* 2001).

## Psychological Factors

There is some evidence that psychological factors play a role in determining cardiovascular health or disease. Stress has been the most widely studied, but additional factors including personality type, a range of negative psychological states and social support have more recently been investigated.

Stress is considered to be a contributory, rather than major risk factor for cardiovascular disease (Powers & Dodd 2003). The exact relationship of stress to cardiovascular disease is currently unclear, but it is generally thought that stress may act either directly through physiological mechanisms, including the effects of stress hormones and prolonged activation of the sympathetic nervous system, or indirectly through unhealthy behavioural changes such as increased smoking (Macleod *et al.* 2002; Powers & Dodd 2003).

Results in this area are inconsistent; while some measures of stress have been significantly associated with cardiovascular morbidity and mortality (e.g. Everson-Rose & Lewis 2005), other measures have not. For example, Heslop *et al.* (2002) found only a limited association between job satisfaction and age-adjusted cardiovascular risk factors in men (no association in women), and no association between job dissatisfaction and cardiovascular disease mortality, despite job satisfaction being a recognised form of stress.

There is also some evidence that personality type can determine the risk of cardiovascular disease. A famous study by Friedman and Rosenman (1974, as cited in Gross 2005) suggested that a particular personality type (Type A) is more strongly associated with coronary heart disease (CHD) than other personality types. 'Type A' individuals characteristically show greater competitiveness, aggressiveness and hostility, and impatience. However, subsequent replications and variations of this study (such as Wellin, Lappas & Wilhelmsen, 2000) have generally not found a link between personality type and risk of cardiovascular disease. It is more likely that the relationship observed by Friedman and Rosenman was due to more negative emotional states experienced by Type A individuals, rather than personality type *per se*. Kubzansky, Davidson and Rozanski (2005) have identified five negative psychological states that have been shown to varying extents to increase cardiovascular disease risk; these are hopelessness, pessimism, rumination, anxiety and anger/hostility.

Lack of social support has been shown to be an independent risk factor for cardiovascular disease (e.g. Everson-Rose & Lewis 2005). Furthermore, social support may also contribute to recovery in people with cardiovascular disease; a longitudinal study by Wellin, Lappas and Wilhelmsen (2000) found that prognosis after myocardial infarction was strongly influenced by a lack of social support (also by depression).

In summary, there is accumulating evidence that cardiovascular health and disease are influenced by psychological factors, but certain factors (such as social support) appear to be of greater importance than others, and there are also inconsistencies in findings. Macleod *et al.* (2002) have criticised the methodology used in many studies of psychological factors and associated cardiovascular outcomes. These researchers have shown that self-report is not a reliable method because participants who report more negative psychological states also tend to report more disease symptoms. This may partially account for the variation in findings, and future studies should therefore use alternative methodologies as much as possible.

It is clear, however, that like physical activity and diet, psychological factors are generally modifiable. It may be possible to improve cardiovascular health and reduce the risk of disease by techniques that reduce stress and improve psychological health, such as relaxation and meditation. Even owning a pet (a form of social support) seems to reduce risk factors for cardiovascular disease (Anderson, Reid & Jennings 1992).

## Conclusion

Cardiovascular health is a product of both genetics and the environment, and is determined by a wide range of variables. Importantly for the prevention and control of cardiovascular disease, the majority of these factors can be modified by lifestyle changes. Although heredity of a predisposition to cardiovascular disease cannot be changed, it is possible to identify individuals who are at risk through genetic counselling, so that appropriate lifestyle changes can then be made (Sturm 2004).

Physical activity is of central importance in the optimisation of cardiovascular health and prevention of disease. Although physical activity is one of the most easily modifiable factors, many people in the Western world lead sedentary lifestyles (Fentem 1994). According to the British Heart Foundation (2006), approximately 70 % of adults in the UK do not meet the recommendations of 30 minutes physical activity 5 times a week. Many studies have established that major cardiovascular benefits are associated with increasing exercise levels (e.g. Williams *et al.* 2003; Noda *et al.* 2005; Hu *et al.* 2005). However, despite the existence of public guidelines for the advised quantity of exercise (e.g. Bouchard, Shephard & Stephens, 1993), there are various inconsistencies in the literature and gaps in our knowledge concerning specific aspects of exercise. Future studies should focus on mode or type, frequency, duration and intensity of exercise (Pescatello *et al.* 2004) in order to refine the current guidelines. There is also a need for further investigation into other modifiable factors that can influence cardiovascular health, but better control of confounding variables (Kelley, Kelley & Tran, 2001), larger sample sizes (Houde & Melillo 2002), and more consistent and objective outcomes (Macleod *et al.* 2002) are necessary.

As morbidity from coronary heart disease and other cardiovascular diseases appears to be increasing in the UK (British Heart Foundation 2006), research in this area clearly remains a major public health priority (Powers & Dodd 2003). Studies that consider the long-term effects on cardiovascular health of lifestyle changes are obviously valuable. For example, a longitudinal study by Paffenbarger *et al.* (1993) showed that moderate physical activity, quitting smoking, maintaining normal blood pressure and avoiding obesity were separately associated with reduced mortality from coronary heart disease (and all causes) in a large sample of men.

Several initiatives that aim to encourage people to adopt healthier lifestyles have been put in place by the government in the UK. These initiatives include the '5 a Day' programme, Local Action Exercise Pilots (LEAPs) and Healthy Living Centres (Department of Health 2006).

As our knowledge of the factors that affect cardiovascular health becomes more elaborated, it will be possible to refine current guidelines and improve both individual and national strategies that incorporate lifestyle changes. This should ultimately lead to a reduction of one of the biggest health burdens of this time, cardiovascular disease.

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