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# Concepts and controversies about the prevention of coronary heart disease

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**Summary**

**Congruent evidence from several medical disciplines provides compelling argument for a preventive approach to atherosclerotic diseases. Intervention trials and community health education programmes are under way. Reasonable, safe and practical approaches are available for hygienic interventions within the medical system. But major impediments to medical and community researches and action in prevention include professional controversy and public confusion about risk factors and their management. It is suggested here that most of this controversy and confusion is unnecessary and much of it due to professional attitudes and experience. These attitudes appear to result from failure to distinguish adequately the risk, diagnosis and therapeutic decisions appropriate to a culture, in the population-at-large.**

## Introduction

Empirical testing of prevention hypotheses in ischaemic heart disease (IHD) is now appropriate, logical and essential. The potential for prevention should be tested in parallel with basic research into mechanisms of atherosclerosis and sudden death. A great strength of western medical systems lies in the tremendous flow of ideas and innovations, in the great openness of expression that are available to all, in one's chances to work effectively in many disciplines, and in the opportunities to read, quote and challenge each other vigorously. Much of the controversy about preventive measures for IHD is due to insufficient information. The cure is more and better data. But perhaps more of it is due to professional attitudes, in which valid observations and decisions for individual patients and their risk may not be appropriate to findings in populations or directions for the public health.

Some of the major controversies in the area of ischaemic heart disease risk factors and prevention will be discussed. They can only be dealt with superficially here—they include diet, hypertension, smoking, activity, stress and heredity. It will also be attempted to enumerate one or two of the professional attitudes and approaches to problems that may be responsible for unnecessary controversy, and which influence to a great extent cardiological thought, training, research and practice.

## Research approaches to prevention

First, it must be made clear that there are three major medical disciplines involved in exploring the nature of ischaemic heart disease and its prevention. The first, in which we are all traditionally involved, is the clinical pathological process; some of us have been trained and experienced in laboratory experimental methodology; far fewer of us are experienced in looking at problems using epidemiology as the basic discipline of preventive medicine and the population outside hospital as a laboratory. Each of these three disciplines provides a needed methodology for the study of disease; all are necessary for the full understanding of the nature and scope of disease; information from each is complementary to the other; none is inherently 'superior' to the other although most medical inspiration comes from observations made on the clinical pathological side.

## Necessity for a preventive approach

Next, as a background for discussing these controversies about prevention of ischaemic heart disease, one must first establish the necessity for attempts at prevention—if there is to be noteworthy progress—based on the fact that clinically one is dealing with end-stage disease. The function of physicians in IHD is largely emergent, palliative and supportive. Estimates about the first year mortality from a first myocardial infarction give the pre-hospital mortality (0–3 hr) somewhere around 25%, in-hospital mortality around 15%, and post-hospital mortality during the first year after the first myocardial infarction something of the order of 10%; the true first year mortality being something of the order of 50%. Ten years hence, what might one expect? A very optimistic estimate of the potential for reduction of mortality with the assumption of a profession highly skilled and devoted, with an

educated public, with emergency facilities and all the technology of coronary care, with the assumption of ventricular assistance, support, conservation and stabilizing devices, one might thereby reduce the first year death rate from myocardial infarcation by another 10%, from 50% to 45% in the next decade. This would be excellent, particularly for those of one's patients (and ourselves) who will be stricken; a large step indeed but hardly a giant leap for mankind.

But there is also a permanent long term excess mortality in IHD which persists 10 years or more after survival from infarction. Finally, in terms of life expectancy, there has not been a great improvement in adult expectancy. Whatever has been gained by affluence and medical advances has been replaced by something else. That 'something else' must be ischaemic heart disease and the other atherosclerotic diseases.

With this background one must remain hopeful and supportive for the individual coronary patient. But, it is possible to become more realistic in terms of what can really be accomplished in prolonging effective life for persons with advanced coronary disease. And one must be distinctly pessimistic in terms of making major inroads on the burden to society of IHD by conventional, supportive, therapeutic medicine when dealing with, in effect, end-stage vascular diseases.

There is a story about the busy practitioner who, taking a breather along the river bank, heard a man hailing from midstream, drowning. The physician shed his coat, jumped in the river, pulled the man ashore, revived him, and just as he was standing up, heard another hail from the middle of the stream and saw another man going down. He repeated the process and, while successfully re-animating the second man, heard a third cry. About this time another physician, a white-coated, epidemiological type, walking along the bank saw the whole scene: the busy, harried physician taking care of a desperate situation, two people recovering, the third crying out desperately for help. And he murmured out loud, 'What do you suppose could be pushing those guys in the river upstream?', to which the busy practitioner replied: 'Don't bother me now, can't you see I have no time to discuss such things!' as he dived into the river for his next resuscitative effort. This connotes in a real sense the situation in medical practice today, that we are desperately concerned and occupied with taking care of the sick and consequently are insufficiently concerned with trying to keep whatever it is from pushing people into the river.

**The potential for prevention**

The basic facts which represent the potential for prevention of ischaemic heart disease are no longer controversial. There are large differences in population frequency and individual risk of IHD. Systematic studies have been made in the Minneapolis laboratory, using standard methods and trained teams and central analysis of the diet, many physical, laboratory and other characteristics of whole populations of men related to their subsequent coronary disease experience. It has been established to the satisfaction of most of the scientific community that men first examined in health and followed-up for years develop vastly different rates of coronary disease, of the order of ten-fold, between Japan and Greece, The Netherlands, U.S.A. and Finland, with Yugoslavia and Italy intermediate. This basic fact, trite and tedious as it was to demonstrate, is nevertheless not trivial in its implications for prevention. It provides the basic potential for prevention. These are not aboriginal populations living on sour milk and berries, or raw fish and blubber, but stable, small-town and rural populations about the world, some of which are not involved at all with manifest coronary disease (Fig. 1).

There is clear evidence from studies about the world that one can rank individuals in apparently good health who indeed have a vastly different risk of developing manifest coronary heart disease (Fig. 2). The stepwise relationship between risk factors and ischaemic heart disease incidence is familiar. Prediction equations which will separate individuals into five to ten times different degrees of future coronary risk according to a multivariate risk score can be computed from the 'big three', hypertension, cigarette smoking and serum cholesterol.

**Controversy about diet**

Much of this controversy is unnecessary and misdirected; it evolves from a basic difference in the physician's clinical approach to problems and the epidemiological approach. It may become clearer if the observations are separated into those of individual cases and their individual risk, and those of the population and its risk, i.e. risk characteristics of a population in distinction to the individual.

Correlations between average saturated fat composition in the habitual diet and average serum cholesterol levels of populations are very strong. In population studies in which diets were analysed systematically and chemically, during all seasons of the year, Keys (1970), showed a correlation of the order of 0·9 between chemically measured diet components and serum cholesterol levels. This correlation is extremely good when measured in an objective fashion in contrasting populations. A different problem is posed by the individual case within a given culture. In this country (Great Britain), for example, people eating the same diet can have different serum lipid levels. This variation is due to

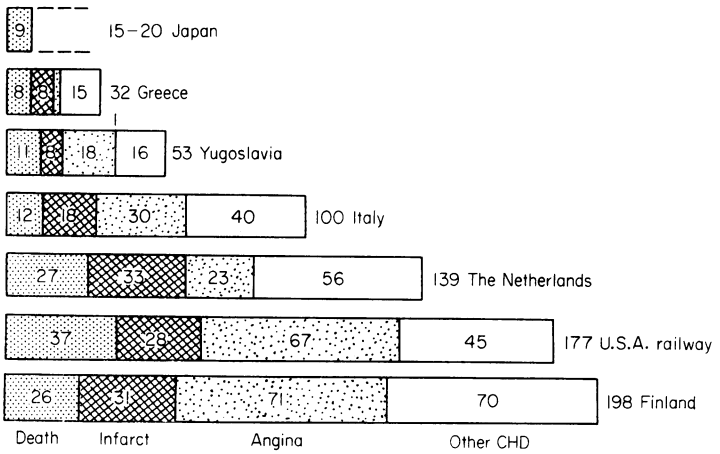


FIG. 1. Age-standardization average yearly CHD incidence rates per 10,000. 12,529 men, aged 40–59 years, judged to be free of CHD at the outset. (Keys, A., ed. (1970) Coronary heart disease in seven countries. By kind permission of the American Heart Association, Inc.)

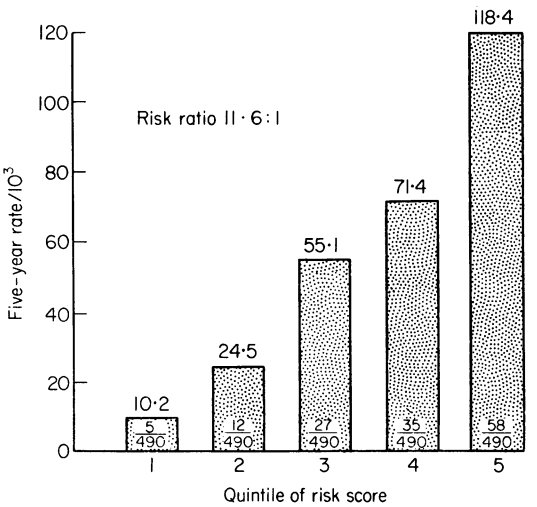


FIG. 2. Combined list factor scale and first coronary event, men aged 40–59 years. *Computed from entry levels of systolic blood pressure, serum cholesterol, and number of cigarettes smoked daily. (Keys, A., ed. (1970) Coronary heart disease in seven countries. By kind permission of the American Heart Association, Inc.)

the intrinsic individual regulation of lipids. But the fact that there are inherent individual differences in the regulation of serum lipids in no way negates the overall importance of a dietary influence on those levels, in the individual, and in entire cultures exposed to habitually excessive eating patterns.

There are several reasons why the correlations, between diet and serum cholesterol levels (or coronary disease), are weak within a given culture, such as within the U.S.A. One is that the measuring tool is extremely poor, a 24-hr recall, or 3 or 7-day diet diaries are simply inadequate ways of measuring the diet of an individual. In using such tools, the variability of diet so measured in the individual is just as large as the variability in diet between individuals. In such a situation, it is mathematically impossible to demonstrate any sharp relationship between the factors being measured, in this case diet and serum cholesterol level. So the tool itself and the natural variation in diet measured prevent an effective study of the question. Moreover, measuring the individual diet once or twice or even four times by such a method is an inadequate measure of the lifelong habitual dietary experience which contributes to serum cholesterol level (and presumably to atherosclerosis). Another important factor is the relative homogeneity of a national diet, e.g. the hallmark of the American way of eating is a high fat, high calorie diet. Comparisons of long term natural diets are more interesting as a means of studying the relationship between diet and serum cholesterol levels. Figure 3 gives the proportion of fat calories in the habitual diets in some population samples from the Seven Countries Study (Keys, 1970), measured chemically in the Minnesota laboratory. The primary difference between fat composition in these countries is in the saturated fat content. The characteristic of countries with high average cholesterol levels and high coronary diseases rates is a saturated fat content exceeding 15% of calories as in the U.S.A., Finland and The Netherlands. The characteristic of countries with extremely low serum cholesterol levels and CHD rates, e.g. Japan and

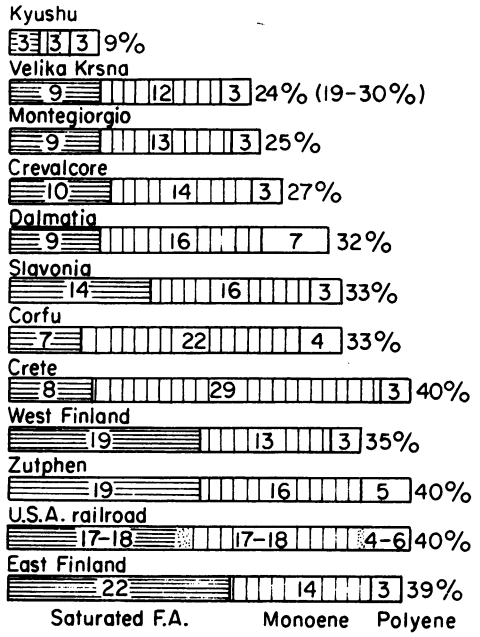


FIG. 3. Average percentage of dietary calories provided by saturated, monoene, and polyunsaturated fatty acids. Men aged 40–59 years. (Keys, A., ed. (1970) Coronary heart disease in seven countries. By kind permission of the American Heart Association, Inc.)

Greece, is saturated fatty acid content under 10% of calories. Again, the correlations between saturated fat and serum cholesterol levels and coronary disease are quite strong. So far as is known, these correlations are not discounted by any other similarly careful and systematic work.

Finally, it can hardly be denied that there is a strong correlation between diet and serum cholesterol if what happens to serum lipid levels from changes in diet is considered. In the Minnesota laboratory, on the basis of over 120 carefully controlled isocaloric substitutions of different fats in the diet, it is possible to predict mathematically the serum cholesterol response from a change in diet in small groups of people, expressed in an equation (2S−P). This indicates that the cholesterol raising power of saturated fatty acids is approximately twice as efficient as the cholesterol lowering power of polyunsaturated fatty acids and that the contribution of dietary cholesterol is significant but may be largely overwhelmed in high fat diets by the saturated fat contribution (Keys, 1967).

*Carbohydrates*

Another controversy concerning diet has to do with carbohydrate composition, carbohydrate-induced hyperlipidaemia and the need for low-carbohydrate diets. This controversy involves singular observations in individual patients within our particular culture and an awareness of experience outside hospital and outside that particular culture. It has been hypothesized that the reduction of fat content of the diet, by increasing the carbohydrate composition, causes hypertriglyceridaemia. Table 1 shows a long-term observation on the Japanese in Japan, Hawaii, and California, genetically similar, in which the frequency of elevated serum cholesterol (< 260 mg/100 ml) varies from $31/10^3$ in Japan, to $124/10^3$ in Hawaii, to $162/10^3$ in the Japanese in California. In the mainland Japanese who subsist on one of the highest carbohydrate diets of civilized industrial nations, the frequency of hypertriglyceridaemia in middle-aged men is of the order of 6% whereas in the Japanese in California on a lower carbohydrate diet, it is of the order of 25%. People subsisting on long term high carbohydrate and low fat diets often do not have hypertriglyceridaemia, on the contrary, they have hypolipidaemia by our standards.

TABLE 1. (a) Prevalence of serum cholesterol elevation (⩾ 260 mg/100 ml in Japanese men * rate/$10^3$

| Age (years) | Japan | Hawaii | California |
|---|---|---|---|
| 45–49 | 27·9 | 131·4 | 138·9 |
| 50–54 | 33·9 | 135·8 | 198·4 |
| 55–59 | 30·6 | 132·7 | 161·0 |
| 60–64 | 27·1 | 127·1 | 160·5 |
| 65·69 | 27·6 | 73·8 | 189·5 |
| Age-adjusted rate | 31·6 | 124·0 | 162·5 |
| No. of men | 2138 | 7961 | 1816 |

TABLE 1. (b) Prevalence of serum triglyceride elevation (⩾ 270 mg/100 ml) in Japanese men * rate/$10^3$

| Age (years) | Japan | Hawaii | California |
|---|---|---|---|
| 45–49 | 79·5 | 272·1 | 278·4 |
| 50–54 | 64·5 | 278·8 | 269·4 |
| 55–59 | 62·0 | 242·9 | 251·9 |
| 60–64 | 38·4 | 180·5 | 262·2 |
| 65–69 | 41·1 | 193·5 | 187·5 |
| Age-adjusted rate | 61·4 | 245·5 | 251·9 |
| No. of men | 1815 | 7658 | 1825 |

* Marmot *et al.*, 1975.

One aspect of the diet sugar controversy will now be considered. Sugar intake is about as highly correlated with coronary disease incidence as is fat intake. The correlation between coronary diseases and saturated fat intake is of the order of 0·86 while the correlation with sugar is of the order of 0·8. However, the correlation of saturated fatty intake with sugar intake is also of the order of 0·8 or 0·9. Could this be another meaningless correlation such as that about the number of telephones and TV

antennae? The point is that there is no congruent evidence between clinical/pathological observations, laboratory/experimental observations, and population/epidemiological evidence to support the sugar hypothesis, as there clearly is in the matter of diet fat and other primary risk characteristics.

*Serum lipids*

In considering serum lipids as risk indicators, it would be apt to quote a distinguished vascular surgeon: 'Most of my vascular disease patients have serum cholesterol levels within the normal range'. This technically correct yet grossly misleading comment may be considered in the light of Fig. 4. Obviously, a whole population may have relatively high lipids; and statistical norms are not ideal norms in terms of risk.

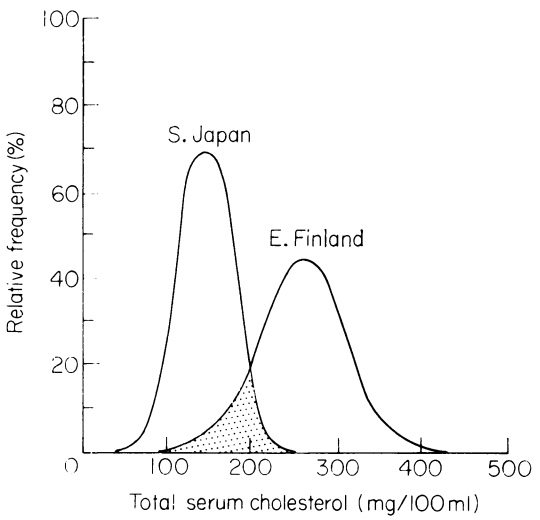


FIG. 4. Distributions of serum cholesterol level in a sample of 504 men aged 40–59 years in Ushibuka, Japan, and 775 men aged 40–59 years in a sample from East Finland. (Keys, A., ed. (1970) Coronary heart disease in seven countries. By kind permission of the American Heart Association, Inc.)

With regard to serum triglycerides, their role in atherogenesis is not yet known nor whether they independently predict coronary incidence. The evidence so far suggests that the very low density lipoproteins provide no predictive evidence independent of that from the low density lipoproteins, but this is not to say that high serum triglycerides are desirable.

**Heredity**

It is important to distinguish between what the observant physician sees in the individual case, and the situation in the population burdened with excess coronary disease. To see a young man, with a strong family history of coronary disease and with a clear-cut familial pattern of hyperlipidaemia, developing early angina pectoris or sudden death impresses one with the role of heredity in that individual; but it is highly improbable that epidemic or mass disease in entire cultures of millions of people can be attributed to inborn metabolic errors of fat metabolism. It is most unlikely that the ten-fold differences between Finland and the U.S.A. versus Japan and the Mediterranean islands could be explained by different hereditary make-up in these peoples. Such distinct hereditary mechanisms are responsible for only a small proportion of the coronary disease in the U.S.A. where there is presumably an unfavourable environmental and cultural situation. There is usually no mass exhibition of inherited traits in the presence of a highly favourable environment. So, despite very great individual differences in intrinsic regulation of serum lipids, or in patterns of the coronary artery circulation, most of the population burden of coronary disease can be attributed to environmental, cultural and potentially modifiable influences—and this national burden is the concern of preventive cardiology.

**High risk detection**

Table 2 illustrates another concept which limits effectiveness of a preventive practice for coronary disease. Note the equivalent risk in this table between the high-risk individual having a serum cholesterol level of 400 mg/100 ml and others. Geoffrey Rose has taken these values directly from Framingham data (Garcia *et al.*, 1974). A man of the same age with a low cholesterol value and a systolic pressure of 250 mmHg has an equivalent risk. In each of these cases, detected on routine examination or screening, the practitioner will be alerted to the high risk status. Yet a third man with a 20 cigarettes/day consumption, whose serum cholesterol and blood pressure levels are a little above average, has as great a coronary risk as the other two, although he is not currently identified as having high risk, either to himself or in the mind of the physician.

TABLE 2. Equivalent coronary risks

| Cigarette smoker | Serum cholesterol (mg%) | Systolic blood pressure |
|---|---|---|
| 0 | 400 | < 120 |
| 0 | < 200 | 250 |
| + | 260 | 140 |

Courtesy of G. Rose, from Framingham data (Section 27, Gordon, Sorlie and Kannel, 1975).

**Behaviour**

There is a large area of controversy concerning stress, personality and behaviour. At one extreme there is the claim that Type A behavioural type is 'the number one cause of heart attack'. It is true that most people feel in their daily lives that stress and behavioural response to stress may have something to do with propensity to sudden death or coronary disease. But, number one cause for whom? For a man whose father died at the age of 38 of a coronary, and who has tendinous xanthomas at the age of 26? It is doubtful that behaviour is his most important risk factor, any more than it is for a man smoking 50 cigarettes per day or for a man with a diastolic pressure of 114 mmHg. What about whole populations such as the calm, delightful civilization of the Finns; can one say that their rate of IHD (the highest on earth) is due to the fact that they are in constant struggle with themselves and their society? At the opposite extreme are the overcrowded, time-urgent, aggressive, ambitious Japanese, not yet touched to any significant degree by the coronary epidemic. Neither from an individual nor a population standpoint can behaviour be 'the most important cause' of coronary disease. Whether or not it operates over and above the main 'known' coronary risk factors is being actively explored. There is now some suggestion that in the U.S.A. culture there may be a small independent contribution of behavioural type to prediction. It remains to be seen whether, if measured, it can be changed, and whether, if changed, this would influence coronary risk, and whether independently, or through action on dietary, smoking or other habits. For the moment, because of the limitations of the measurement and the failure to demonstrate whether behaviour can be successfully modified, the hypothesis remains an interesting, but still an untestable one. For the moment, in preventive trials and community programmes those risk factors for which the influence is clearly shown, which are clearly measurable, and clearly modifiable, must be pursued.

**Physical activity**

Physical activity is one of the more controversial of risk elements because it is very difficult to measure, or to modify experimentally, or to modify as a single risk factor. A number of investigators have pondered the problem of physical activity in coronary disease, have reviewed all the data on occupational and leisure time comparisons, and have come to the conclusion that most of the data are consistent with a relatively slight protective effect of activity. But in none of the studies is the design satisfactory. In none of the studies is it possible to eliminate bias, i.e. to be sure that the groups compared are similar in characteristics other than those of leisure or occupational activity. It is the opinion of a number of investigators that a test of the activity hypothesis in primary prevention of coronary disease is not feasible in our time. We are thus left to extrapolate from our knowledge about the importance of locomotion and large muscle endurance activity and its tonic effect on the body, its psychic influence, its role in terms of energy balance, weight control and prevention of obesity, and to recommend moderation and regularity, without hesitation, for these reasons rather than for scientific certainty that we are influencing the course of atherosclerosis or the likelihood of coronary event in our patients.

**Other professional attitudes**

Finally, let us consider a few other professional attitudes about prevention. The author does not believe that a 'scientific breakthrough' is just around the corner which will make it possible for atheroma to be dissolved or resolved, or for hypertension completely to be eliminated. It is maintained that balanced efforts should be made towards both sound attempts at prevention and basic research.

One issue should indeed be faced squarely; imagine that the preventive measures do not prove very effective in high risk middle-aged groups in which they are being tested in the U.S.A. and Europe, in multiple risk factor intervention trials. Similarly, the results may not be impressive in tests of secondary prevention in post-infarction survivors such as in the Coronary Drug Project, the current studies on coronary artery surgery on ileal by-pass in myocardial infarction patients, and on physical fitness and rehabilitation of coronary patients. There is little reason to expect that intervention on single primary risk factors at manifest and advanced stages of atherosclerotic disease could greatly reduce the rate of coronary events or sudden death, which must to a far greater degree be determined by the vascular and myocardial damage than by specific precipitating or atherogenic factors. If prevention trials were started at ages where prevention might be expected to be more influential in terms of the atherosclerotic process, there would exist the virtually impossible requirement of extremely long-term studies on young people.

Clearly, basic research must be continued at a high level. It remains to be seen whether the prevention trial results are definitively positive, or suggestive of a trend, or otherwise. If positive, it will probably be possible to move promptly into the broader public health application of preventive measures. If, however, the results are clearly negative, in the very high risk, this would not disprove the major multiple risk factor hypothesis about the causes of ischaemic heart disease and atherosclerosis,

so clearly set out in other clinical, pathological and epidemiological evidence. It is considered unlikely that multifactor primary intervention on smoking habit, blood pressure and blood lipid levels in high risk groups will prove wholly ineffective.

**Social changes**

Finally, the author is inclined to be somewhat optimistic in terms of eventually changing professional and social attitudes along the lines of prevention. It is even possible to observe today all sorts of hostile and aggressive behaviour which are more socially acceptable in this medical meeting than is cigarette smoking. Better ways are needed to encourage our patients not to smoke, but there is no doubt that professional attitudes will change as the population picture becomes more clear, when and if definitive evidence is gathered from the trials. The exciting 'Three Town Study' by Stanford University suggests already that use of the media combined with screening and intervention on a target group of high risk individuals will effect substantial changes in attitudes, behaviour, and risk factor levels in the community as a whole (Haskell *et al.*, 1974).

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