

## [The Cholesterol Myths](#) by [Uffe Ravnskov, M.D., Ph.D.](#)

### **1. Your cholesterol tells very little about your future health**

Cholesterol is a peculiar molecule. It is often called a lipid or a fat. However, the chemical term for a molecule such as cholesterol is alcohol, although it doesn't behave like alcohol. Its numerous carbon and hydrogen atoms are put together in an intricate three dimensional network, impossible to dissolve in water. All living creatures use this indissolvability cleverly, incorporating cholesterol into their cell walls to make cells waterproof. This means that cells of living creatures can regulate their internal environment undisturbed by changes in their surroundings, a mechanism vital for proper function. The fact that cells are waterproof is especially critical for the normal functioning of nerves and nerve cells. Thus, the highest concentration of cholesterol in the body is found in the brain and other parts of the nervous system.

Because cholesterol is insoluble in water and thus also in blood, it is transported in our blood inside spheric particles composed of fats (lipids) and proteins, the so-called lipoproteins. Lipoproteins are easily dissolved in water because their outside is composed mainly of water-soluble proteins. The inside of the lipoproteins is composed of lipids, and here are room for water-insoluble molecules such as cholesterol. Like submarines, lipoproteins carry cholesterol from one place in the body to another.

The submarines, or lipoproteins, have various names according to their density. The best known are HDL (High Density Lipoprotein), and LDL (Low Density Lipoprotein). The main task of HDL is to carry cholesterol from the peripheral tissues, including the artery walls, to the liver. Here it is excreted with the bile, or used for other purposes, for instance as a starting point for the manufacture of important hormones. The LDL submarines mainly transport cholesterol in the opposite direction. They carry it from the liver, where most of our body's cholesterol is produced, to the peripheral tissues, including the vascular walls. When cells need cholesterol, they call for the LDL submarines, which then deliver cholesterol into the interior of the cells. Most of the cholesterol in the blood, between 60 and 80 per cent, is transported by LDL and is called "bad" cholesterol, for reasons that I shall explain soon. Only 15-20 percent is transported by HDL and called "good" cholesterol. A small part of the circulating cholesterol is transported by other lipoproteins.

You may ask why a natural substance in our blood, with important biologic functions, is called "bad" when it is transported from the liver to the peripheral tissues by LDL, but "good" when it is transported the other way by HDL. The reason is that a number of follow-up studies have shown that a lower-than-normal level of HDL-cholesterol and a higher than-normal level of LDL-cholesterol are associated with a greater risk of having a heart attack, and conversely, that a higher-than-normal level of HDL-cholesterol and a lower-than normal LDL-cholesterol are associated with a smaller risk. Or, said in another way, a low HDL/LDL ratio is a risk factor for coronary heart disease.

However, a risk factor is not necessarily the same as the cause. Something may provoke a heart attack and at the same time lower the HDL/LDL ratio. Many factors are known to influence this ratio.

#### **What is good and what is bad?**

People who reduce their body weight also reduce their cholesterol. In a review of 70 studies Dr. Anne Dattilo and Dr. P.M. Kris-Etherton concluded that, on average, weight reduction lowers cholesterol by about 10 per cent, depending on the degree of the reduction. Interestingly, it is only cholesterol transported by LDL that goes down; the small part

transported by HDL goes up. In other words, weight reduction increases the ratio between HDL- and LDL-cholesterol (1). An increase of the HDL/LDL ratio is called "favorable" by the diet-heart supporters; cholesterol is changed from "bad" to "good". But is it the ratio or the weight reduction that is favorable? When we become fat, other harmful things occur to us. One is that our cells become less sensitive to insulin, so that some of us develop diabetes. And people with diabetes are much more likely to have a heart attack than people without diabetes, because atherosclerosis and other vascular damage occur very early in diabetics, even in those without lipid abnormalities. In other words, overweight may increase the risk of a heart attack by mechanisms other than an unfavorable lipid pattern, while at the same time overweight lowers the HDL/LDL ratio.

Also smoking increases cholesterol a little. Again, it is LDL-cholesterol that increases, while HDL-cholesterol goes down, resulting in an "unfavorable" HDL/LDL ratio (2). What is certainly unfavorable is the chronic exposure to the fumes from burning paper and tobacco leaves. Instead of considering the low HDL/LDL ratio as bad it could simply be smoking itself that is bad. Smoking may provoke a heart attack and, at the same time, lower the HDL/LDL ratio.

Exercise decreases the bad LDL-cholesterol and increases the "good" HDL-cholesterol (3). In well-trained individuals the "good" HDL is increased considerably. In a comparison between distance runners and sedentary individuals, Dr. Paul D. Thompson and his colleagues found that the athletes on average had a 41 per cent higher HDL-cholesterol level (4). Most population studies have shown that physical exercise is associated with a lower risk of coronary heart disease, and a sedentary life with a higher risk. It also seems plausible that a well-trained heart is better guarded against obstruction of the coronary vessels than a heart always working at low speed. A sedentary life may predispose people to a heart attack and, at the same time, lower the HDL/LDL ratio.

A low ratio is also associated with high blood pressure (5). Most probably, the hypertensive effect is created by the sympathetic nerve system, which is often overstimulated in hypertensive patients. Hypertension (or too much adrenalin) may provoke a heart attack, for instance by inducing spasm of the coronary arteries or by stimulating the arterial muscle cells to proliferate, and, at the same time, lower the HDL/LDL ratio.

### **Univariate and multivariate**

As you see, it is not easy to know what is bad. Is it bad to be fat, to smoke, to be inactive, to have high blood pressure, or to be stressed? Or is it bad to have a lot of bad cholesterol? Or both? Is it good to be slim, to stop smoking, to exercise, to have normal blood pressure, to be emotionally calm? Or is it good to have much "good" cholesterol? Or both? Thus, the risk of having a heart attack is greater than normal for people with high LDL-cholesterol, but so is the risk for fat, sedentary, smoking, hypertensive and mentally stressed individuals. And since such individuals usually have elevated levels of LDL-cholesterol, it is, of course impossible to know whether the increased risk is due to the previously mentioned risk factors (or to risk factors we do not yet know) or to the high LDL-cholesterol. A calculation of the risk of high LDL-cholesterol that ignores other risk factors is called a univariate analysis and is, of course, meaningless.

To prove that high LDL-cholesterol is an independent risk factor, we should ask if fat, sedentary, smoking, hypertensive and mentally stressed individuals with a high LDL-cholesterol level are at greater risk for coronary disease than fat, sedentary, smoking, hypertensive and mentally stressed individuals with low or normal LDL cholesterol.

Using complicated statistical formulas, it is possible to do such comparisons in a population of individuals with varying degrees of the risk factors and varying levels of LDL-cholesterol, a so-called multivariate analysis. If a multivariate analysis of the prognostic value of LDL cholesterol

also takes body weight into consideration, it is said to be "adjusted for body weight". A major problem with such calculations is that we know a great number of risk factors because the more risk factors that are adjusted for, the less reliable the result will be. Another problem is that the data generated by these and other complicated statistical methods are almost impossible for most readers, including most physicians, to comprehend. For many years researchers in this area have not presented primary data, simple means, or simple correlations. Instead, their papers have been salted with meaningless ratios, relative risks, p-values, not to mention obscure concepts such as the standardized logistic regression coefficient, or the pooled hazard rate ratio. Instead of being an aid to science, statistics are used to impress the reader and cover the fact that the scientific findings are trivial and without practical importance. Nevertheless, let us have a look at some of the studies.

### **The "good" one**

Publications almost beyond counting have studied the prognostic value of the "good" HDL-cholesterol. The reason is, of course, that it is hard to find any prognostic value. If HDL-cholesterol had a heart-protecting effect of real importance, it would not be necessary to use the tax payers' money to demonstrate the effect again and again in expensive studies. To be brief I shall tell you only about a few of the largest studies.

In 1986 the medical statistician, Dr. Stuart Pocock and his coworkers published a report concerning more than 7000 middle-aged men in 24 British towns (6). The men had been followed for about four years after a detailed analysis of their blood lipids. During this period 193 of the men had had a heart attack. As in most previous studies, these men had on average a lower HDL-cholesterol at the beginning than the men who did not have a heart attack. The mean difference between the cases and the other men was 2.7 mg/dl, or about 6 per cent. This difference was small of course, but thanks to the large number of individuals studied it was statistically significant.

But this was a univariate analysis and as mentioned, the difference could therefore be explained by many ways. A multivariate analysis adjusted for age, blood pressure, body weight, cigarette smoking and non-HDL-cholesterol reduced the difference to an insignificant 0.9 mg/dl, or 2 per cent. This means that those who had suffered a heart attack had a lower HDL-cholesterol mainly because they were older, fatter, had a higher blood pressure and smoked more than those who had not had a heart attack. Dr. Pocock and his colleagues concluded that a low HDL-cholesterol level is not a major risk factor for coronary heart disease.

Their results were challenged in 1989 by nine American scientists headed by Dr. David Gordon. They had analysed the predictive value of HDL-cholesterol in four large American studies, a total of more than 15,000 men and women (7). They thought that the British scientists had used an incorrect way to adjust their figures. If another formula is used, the American researchers wrote, HDL-cholesterol is a much better predictor.

But in one of the four studies, analyzed by Dr. Gordon and his colleagues, the number of fatal heart attacks was identical in the first and second HDL tertile (individuals were classified into three groups, or tertiles, according to their HDL-cholesterol). In one of the studies the number of fatal cases was identical in the second and the third tertile, and in one study more deaths were seen in the third tertile (those who had the largest amount of the "good" cholesterol) than in the second tertile. And these figures were the unadjusted ones.

After adjustment for age, cigarette smoking, blood pressure, body weight and LDL-cholesterol the differences were even smaller. In three of the four studies, the differences lost statistical significance. And remember that the figures were not adjusted for physical activity or mental stress, not to mention the risk factors we do not know yet.

Dr. Pocock and his colleagues returned with a new analysis later the same year, now using the same way of analysing as had Dr. Gordon and his colleagues. At that time the participants in the study had been followed for 7.5 years and a total of 443 heart attacks had occurred. This is the largest single HDL study to date [\(8\)](#).

This time a difference was noted between the HDL cholesterol of the heart patients and the others. The difference was small but statistically significant, even after adjustment for the five risk factors mentioned. However, the largest difference was noted for total cholesterol. The authors therefore concluded that a determination of HDL-cholesterol may be of marginal additional value in screening and in intervention programs for risk of coronary heart disease. They could also have added that they did not adjust for all risk factors so that the difference could as well be due to the heart patients being, for instance, more stressed or less active physically than the others.

### **The "bad" one**

"LDL has the strongest and most consistent relationship to individual and population risk of CHD, and LDL-cholesterol is centrally and causally important in the pathogenetic chain leading to atherosclerosis and CHD". These words you will find in the large review Diet and Health [\(9\)](#).

Reviews by distinguished scientific bodies are supposed to meet high standards. Therefore, you are probably wondering how the authors of Diet and Health, an official, most authoritative and supposedly reliable review from the National Research Council in Washington, had reached their conclusion about LDL-cholesterol. Four publications were mentioned.

In 1973 Dr. Jack Medalie and his coworkers published a five-year follow-up study of 10,000 Israeli male government and municipal employees [\(10\)](#). But the Israeli study did not support the words of Diet and Health, because total cholesterol, not LDL-cholesterol, had the strongest relationship to risk of coronary disease.

The second paper claimed by the Diet and Health-authors was a 1977 report from the Framingham Study by Dr. Tavia Gordon and her colleagues [\(11\)](#). This study concerned HDL cholesterol, however. Only logistic regression coefficients (a statistical concept unknown to most doctors) for coronary disease on LDL-cholesterol were given, and one of the conclusions of the paper was that "LDL-cholesterol ...is a marginal risk factor for people of these age groups" (men and women above 50 years). Some of the coefficients were indeed low. For women above the age of 70 it was negative, which means that women at that age ran a greater risk of having a heart attack if their LDL-cholesterol was low than if it was high. Thus, there was no support either from Gordon's paper.

Also, the third paper [\(12\)](#) concerned HDL-cholesterol only. No support again.

The fourth reference was to the National Cholesterol Education Program, which produced another large review without original data [\(13\)](#). One of its conclusions was that "a large body of epidemiologic evidence supports a direct relationship between the level of serum total and LDL-cholesterol and the rate of CHD." The large body of evidence was to be found in three references. The first one was another large review without original data, Optimal resources for primary prevention of atherosclerotic disease [\(14\)](#), with Dr. Kannel as the first author. I shall return to their review below.

The next reference was yet a large review [\(15\)](#), but nothing in that review was said about the connection between the LDL-level and the incidence of coronary heart disease.

The last reference was an analysis of various lipoproteins as risk factors in the Honolulu Heart Study (16). The conclusion of that paper was that "both measures of LDL-cholesterol were related to CHD prevalence, but neither appeared to be superior to total cholesterol".

Before I discuss Kannel's review I shall mention another conclusion in the National Cholesterol Education Program: "The issue of whether lowering LDL-cholesterol levels by dietary and drug interventions can reduce the incidence of CHD has been addressed in more than a dozen randomized clinical trials". This is a most misleading statement because at that time, in 1988, only four randomized trials including LDL-cholesterol analysis had previously been published (17), and only in one of them the number of heart attacks was lowered significantly.

Let me now return to the review by Kannel and colleagues, the one used as evidence by the authors of The Cholesterol Education Program, which in turn was used as evidence by the authors of Diet and Health. Almost nothing was written about LDL-cholesterol in Kannel's review except for the following (page 164A): "Longitudinal studies within populations show a consistent rise in the risk of CHD in relation to serum total cholesterol and LDL-cholesterol at least until late middle-age".

A little more cautious conclusion than in Diet and Health, it may seem, but even for this prudent statement the evidence was weak. References to six studies were given. In two of them LDL-cholesterol was not analysed or mentioned at all (18); in two reports LDL-cholesterol was only correlated to the prevalence of heart disease (19); in one report two tables were aimed at the subject (tables 8 and 9) and showed that the predictive power of LDL-cholesterol was statistically nonsignificant (20); in one study LDL-cholesterol was predictive for heart disease, but only for men between 35 and 49 and for women between 40 and 44 (21).

In conclusion, the "large body of evidence" was cooked down to one single study, which showed a predictive value for LDL-cholesterol but for a few age groups only. LDL-cholesterol is neither centrally nor causally important, it has not the strongest and most consistent relationship to risk of CHD, it has not a direct relationship to the rate of CHD, and it has not been studied in more than a dozen randomized trials.

But how then has the idea of the bad cholesterol emerged? As mentioned in the National Cholesterol Education Program, there are two main reasons. First, there was the discovery of a defective LDL-receptor in familial hypercholesterolemia and its consequence, the extremely high level of LDL-cholesterol in the blood of individuals with this disease. The discoverers, Nobel prize winners Michael Brown and Joseph Goldstein, suggested that the high LDL-cholesterol was the direct cause of the vascular changes seen in such individuals and also suggested that a similar mechanism was operating in the rest of us (22). Second, feeding experiments in animals raised the animals' LDL-cholesterol and produced vascular changes that have been called atherosclerosis by the experimentators.

These arguments are weak, however. If LDL-cholesterol were the devil himself LDL-cholesterol would clearly be a better predictor than total cholesterol, because the latter include also the "good" HDL-cholesterol. And experiments on animals can only be suggestive and cannot prove anything about human diseases. Besides, the vascular findings in laboratory animals do not look like human atherosclerosis at all, and it is impossible to induce a heart attack in animals by diet alone (23). And finally, findings pertaining to people with a rare genetic error in cholesterol metabolism are not necessarily valid for the rest of us (24).

Thus, the experimentors claim support from unsupportive epidemiological and clinical studies, and the epidemiologists and the clinicians claim support from inconclusive experimental evidence. The victims of this miscarriage of justice are an innocent and useful molecular construction in our blood, producers and manufacturers of animal fat all over the world, and

millions of healthy people who are frightened and badgered into eating a tedious and flavorless diet that is said to lower their bad cholesterol.

## 2. Blood cholesterol has nothing to do with atherosclerosis

One of the most surprising facts about cholesterol is that there is no relationship between the blood cholesterol level and the degree of atherosclerosis in the vessels. If a high cholesterol really did promote atherosclerosis, then people with a high cholesterol should evidently be more atherosclerotic than people with a low. But it isn't so.

The pathologist Dr. Kurt Landé and the biochemist Dr. Warren Sperry at the Department of Forensic Medicine of New York University were the first to study that question (25). The year was 1936. To their surprise, they found absolutely no correlation between the amount of cholesterol in the blood and the degree of atherosclerosis in the arteries of a large number of individuals who had died violently. In age group after age group their diagrams looked like the starry sky.

Drs. Landé and Sperry are never mentioned by the proponents of the diet-heart idea, or they misquote them and claim that they found a connection (26), or they ignore their results by arguing that cholesterol values in the dead are not identical with those in living people.

That problem was solved by Dr. J. C. Paterson from London, Canada and his team (27). For many years they followed about 800 war veterans. Over the years, Dr. Paterson and his coworkers regularly analyzed blood samples from these veterans. Because they restricted their study to veterans who had died between the ages of sixty and seventy, the scientists were informed about the cholesterol level over a large part of the time when atherosclerosis normally develops.

Dr. Paterson and his colleagues did not find any connection either between the degree of atherosclerosis and the blood cholesterol level; those who had had a low cholesterol were just as atherosclerotic when they died as those who had had a high cholesterol.

Similar studies have been performed in India (28), Poland (29), Guatemala (30), and in the USA (31), all with the same result: no correlation between the level of cholesterol in the blood stream and the amount of atherosclerosis in the vessels.

But a correlation has been found in a few studies. One of these was the famous study from Framingham, Massachusetts (32). The correlation found by the Framingham investigators was minimal, however. In statistical terms, the correlation coefficient there was only 0.36. Such a low coefficient indicates a desperately weak relationship between variables, in this case, of course, between cholesterol and atherosclerosis. Usually, scientists demand a much higher correlation coefficient before they conclude that there is a biologically important relationship between two variables.

The very low correlation coefficient was arrived at after much study. First, many of the townspeople of Framingham had their cholesterol tested several times over a period of several years. Then, Dr. Manning Feinleib of the National Heart, Lung, and Blood Institute, led a team of coworkers in studying the coronary vessels of those who had died. The researchers were eager to learn which of the many factors they had studied was most important in the development of atherosclerosis in these dead people from Framingham. Was it blood cholesterol or the number of cigarettes smoked, or something else?

After carefully describing the atherosclerosis in the coronary arteries of the dead people, Dr. Feinleib and his associates concluded that the cholesterol level of the blood best predicted the

degree of atherosclerosis. Neither age nor weight nor blood pressure nor any other factor was as good as blood cholesterol. But again, the correlation coefficient between cholesterol and atherosclerosis was a mere 0.36.

The written report of the study offered no diagrams and no information about the cholesterol and atherosclerosis of each of the individuals whose bodies had been examined. And the report did not discuss the very low correlation coefficient; it didn't even comment upon that matter.

When scientists reach a result contrary to all previous studies, it is routine--not merely usual but routine--to provide a detailed report about the result and also to discuss any possible ways in which the study may have been biased away from accuracy and truth. In the Framingham case, there was an especially great need for this routine scientific procedure to be followed. Not only was the correlation coefficient so trivial, but this study, funded with millions of taxpayers' dollars by The National Institute of Health, could have a major impact on national health care and the American economy. If there was no connection between cholesterol and atherosclerosis, as the previous studies had shown, then there was no reason to bother about cholesterol or the diet. And billions of taxpayers' dollars could have been spent more wisely than in lowering the cholesterol of healthy people.

But the scientists conducting the Framingham study had no reservations. They were eager to stress their own excellence and to highlight the weaknesses of Dr. Paterson's study of Canadian war veterans. In their report, they did not mention the studies of Drs. Landé and Sperry at all, nor the studies from India, Poland, Guatemala or the USA. When the Framingham study authors mentioned their opponents, it was only to criticize without putting their own cards on the table. Some of those hidden cards are fascinating to wonder about.

How were the dead of Framingham chosen for postmortem examination, for example? From 914 dead individuals, the researchers examined only 281. And from the 281, they selected 127 (14 per cent of all dead) who became the subjects of an autopsy program especially designed to investigate the heart and its vessels.

Thus, those chosen for autopsy in the Framingham study were not a random sampling of the population, as they had been in the previous studies. The report from Framingham said nothing about the selection criteria, although scientific studies routinely do. Usually the determining factor is age. A postmortem is seldom performed on people who have died peacefully in old age, as most of us will. Primarily, a postmortem is restricted to young and middle-aged people, who have died before their time, and so it was in the Framingham study. Almost half of those autopsied were younger than 65 years. For this reason, the autopsied subjects had to have included a relatively large number with familial hypercholesterolemia, the unusual genetic disease of cholesterol metabolism. Furthermore, people with this disease are of special interest to scientists studying the cholesterol problem and were probably chosen for autopsy in a program tailored to investigate coronary disease.

With only 14% of the Framingham dead chosen for autopsy, the risk of bias must have been great because there is one exception from the above rule: patients with the rare disease familial hypercholesterolemia have much atherosclerosis, and very high cholesterol levels in their blood. If many such patients are included in a study of cholesterol and atherosclerosis, a correlation will be found.

The question about blood cholesterol and atherosclerosis has been studied by coronary angiography also. It seems as if every specialist in coronary angiography in America has performed his own study, funded with federal tax money awarded by the National Heart, Lung and Blood Institute. In paper after paper published in various medical journals, using almost identical words, these medical specialists emphasize the importance of the blood cholesterol level for the development of atherosclerosis ([33](#)).

But the reports offer no individual figures, only correlation coefficients, and these are never above a minimal 0.36, usually even smaller. And they never mention any of the previous studies that found no association between degree of atherosclerosis and level of blood cholesterol.

Studies based on coronary angiography are fundamentally flawed if their findings are meant to be applied to the general population. Coronary angiographies are performed, mainly, on young and middle-aged patients with symptoms of heart disease, which means that a relatively large number of patients with familial hypercholesterolemia must have been included. Again, there is an obvious risk for the kind of bias that I described above. The fact that this objection is justified was demonstrated in a Swedish study performed by Dr. Kim Cramér and his group in Gothenburg, Sweden (34). As in most other angiographic studies the patients with the highest cholesterol values had on average the most arteriosclerotic coronary vessels.

But if those who were treated with cholesterol-lowering drugs were excluded, and almost certainly this group must have included all patients with familial hypercholesterolemia, the correlation between blood cholesterol and degree of atherosclerosis disappeared.

In Japan the food is meager, blood cholesterol is low and the risk of getting a heart attack is much smaller than in any other country. Given these facts you will most probably say that in Japan atherosclerosis must be rare.

The condition of the arteries of American and Japanese people was studied in the fifties by Professors Ira Gore and A. E. Hirst at Harvard Medical School (35) and Professor Yahei Koseki from Sapporo, Japan. At that time US people on average had a blood cholesterol of 220 whereas Japanese had about 170.

The aorta, the main artery of the body, from 659 American and 260 Japanese people were studied after death. Meticulously all signs of atherosclerosis were recorded and graded. As expected, atherosclerosis increased from age 40 and upwards, both in Americans and in Japanese. Now to the surprising fact.

When degree of atherosclerosis was compared in each age group there was hardly any difference between American and Japanese people. Between age forty and sixty Americans were a little more arteriosclerotic than Japanese; between sixty and eighty there was practically no difference, and above eighty Japanese were a little more arteriosclerotic than Americans.

A similar study was conducted by Dr J.A. Resch from Minneapolis and Dr.s N. Okabe and K. Kimoto from Kyushu, Japan (36). They studied the arteries of the brain in 1408 Japanese and in more than 5000 American people and found that in all age groups Japanese people were more arteriosclerotic than were Americans.

The conclusion from these studies is of course that the level of cholesterol in the blood has little importance for the development of atherosclerosis, if any at all.

Read also:

U. Ravnskov. [Is atherosclerosis caused by high cholesterol?](#) published in Quarterly Journal of Medicine (2002; 95: 397–403)

### 3. The diet has little to do with your blood cholesterol level

A reduction of animal fat and an increase of vegetable fat in the diet is said to lower the blood cholesterol. This is correct, but the effect of such dietary changes is very small. Ramsay and Jackson (37) reviewed 16 trials using diet as intervention. They concluded that the so-called step-I diet, which is similar to the dietary advices that are given nationwide by the health authorities in many countries, lower the serum cholesterol by 0 to 4% only. There are more effective diets, but they are unpalatable to most People.

Studies of African tribes have shown that intakes of enormous amounts of animal fat not necessarily raises blood cholesterol; on the contrary it may be very low. Samburu people, for instance, eat about a pound of meat and drink almost two gallons of raw milk each day during most of the year. Milk from the African Zebu cattle is much fatter than cow's milk, which means that the Samburus consume more than twice the amount of animal fat than the average American, and yet their cholesterol is much lower, about 170 mg/dl (38).

According to the view of the Masai people in Kenya, vegetables and fibers are food for cows. They themselves drink half a gallon of Zebu milk each day and their parties are sheer orgies of meat. On such occasions several pounds of meat per person is not unusual. In spite of that the cholesterol of the Masai tribesmen is among the lowest ever measured in the world, about fifty percent of the value of the average American (39).

Shepherds in Somalia eat almost nothing but milk from their camels. About a gallon and a half a day is normal, which amounts to almost one pound of butter fat, because camel's milk is much fatter than cow's milk. But although more than sixty percent of their energy consumption comes from animal fat, their mean cholesterol is only about 150 mg/dl, far lower than in most Western people (40).

Proponents of the diet-heart idea say that these African tribesmen are accustomed to their diet and that their organisms have inherited a cleverness to metabolize cholesterol. However, a study of Masai people who had lived for a long time in the Nairobi metropolis showed this to be wrong (41). If the low cholesterol of the Masai tribesmen was inherited it should have been even lower in Nairobi, because here their diet with all certainty included less animal fat than the diet of the Masai tribesmen. But the mean cholesterol level in twenty six males in Nairobi was twenty-five percent higher than that of their cattle-breeding colleagues in the countryside.

And there is more evidence. Although it is possible to change blood cholesterol a little in laboratory experiments and clinical trials by dieting, it is impossible to find any relationship between the make up of the diet and the blood cholesterol of individuals who are not participating in a medical experiment. In other words, individuals who live as usual and eat their food without listening to doctors or dieticians show no connection between what they eat and the level of their blood cholesterol.

If the diet-heart idea were correct individuals who eat great amounts of animal fat would have higher cholesterol than those who eat small amounts; and individuals who eat small amounts of vegetable fat should have higher cholesterol than those who eat great amounts. If not, there is no reason to meddle with people's diet.

In the early 1950's the Framingham study included dietary analyses. Almost one thousand individuals were questioned in detail about their eating habits. No connection was found between the composition of the food and the cholesterol level of the blood. Wrote Drs. William Kannel and Tavia Gordon, authors of the report: "These findings suggest a cautionary note with respect to hypotheses relating diet to serum cholesterol levels. There is a considerable range of serum cholesterol levels within the Framingham Study Group. Something explains this

inter-individual variation, but it is not diet." For unknown reasons, their results were never published. The manuscript is still lying in a basement in Washington.

In a small American town called Tecumseh, Michigan a similar study was performed by a team of researchers from the University of Michigan headed by Dr. Allen Nichols [\(42\)](#). Experienced dieticians asked in great detail more than two thousand individuals what they had eaten during a twenty-four hour period. The dieticians also asked about the ingredients of the food, analysed the recipes of home-cooked dishes, and exerted great care to find out what kind of fat was used in the kitchen. Calculations were then performed using an elaborate list of the composition of almost 3000 American food items. Finally the participants were divided into three groups, a high, a middle, and a low level group, according to their blood cholesterol.

No difference was found between the amounts of any food item in the three groups; of special interest was that those with a low blood cholesterol ate just as much saturated fat as did those with a high cholesterol.

These studies concerned adults, but no association has been found in children either. At the famous Mayo Clinic in Rochester, Minnesota, for instance, Dr. William Weidman and his team analyzed the diet of about one hundred school children [\(43\)](#). Great differences were found between the amount of various food items eaten by these children, and also great differences between their blood cholesterol values, but there wasn't the slightest connection between the two. The children who ate lots of animal fat had just as much or just as little cholesterol in their blood as the children who ate very little animal fat. A similar investigation of 185 children was performed in New Orleans with the same result [\(44\)](#).

Even if no pains are spared to investigate the diet of people the information gathered is of course uncertain. Who can recall everything that he has eaten in the last twenty four hours? And the diet of one 24-hour period may not be representative of the usual diet of the individual. A better result can be achieved by studying the diet over several days, preferably during various seasons of the year. In London professor Jeremy Morris and his team used this method and asked ninety-nine middle-aged male bank staff members to weigh and record what they ate over two weeks [\(45\)](#).

Have you ever bargained in a bank? Maybe you will succeed in the director's office, but certainly not at the teller's counter. If anyone is scrupulous with nickels and dimes, it is those sitting behind the glass of the bank.

Ninety-nine of these honorable men were asked to sit at home with a letter balance and weigh every morsel they ate for a whole week. But again, this meticulous method revealed no connection either between the food and the blood cholesterol level.

To be certain, seventy-six of the bank men repeated the procedure for another week at another time of the year: no connection was found, once again.

To be absolutely certain the researchers selected those whose records were especially detailed and accurate. Once more, no connection was found.

On average, Finnish people have the highest cholesterol in the world. According to the diet-heart idea's proponents, this is due to the fat-rich Finnish food. The answer is not that simple, however. This was demonstrated by Dr. Rolf Kroneld and his team at the University of Turku [\(46\)](#). They studied all inhabitants of the village of Iniö near Turku, and twice as many randomly selected individuals of the same age and sex in North Karelia and in southwest Finland.

Apparently a health campaign had struck Iniö. There the consumption of margarine was twice as great and the consumption of butter only half as what it was in the other places. Also, the people of Iniö preferred skimmed over more fat milk; the residents in the other places did not. But the highest cholesterol values were found in Iniö. The average value for male Iniö inhabitants was 283, on the two other places it was 239 and 243 mg/dl. Regarding women, the difference was still greater.

Is it really wise to meddle with people's dietary habits if their food has no influence on their cholesterol? And how do those who believe that fat food is dangerous explain all these negative results?

The most common objection says that information about dietary habits is inaccurate, and it is. But even if it is uncertain what people say they ate yesterday, a crude relationship should appear if a sufficiently large number of individuals were questioned meticulously. If not, the influence of the diet, if any, is so minute that it cannot possibly have any importance.

Diet-heart supporters also argue that most people in Western communities already eat great amounts of fat and cholesterol. This argument declares that we have already crossed a threshold of too much animal fat in the diet so that more fat does not make any impact on our blood cholesterol.

The argument is in conflict with the studies I have mentioned above. For instance, astonished by their negative results Dr. Nichols and his team from Michigan (42) tried to find explanations. But they did not find that all individuals ate much fat. Wrote the authors: "The distribution of daily intake of total fat, saturated fat, and cholesterol by the individuals in this study was quite broad".

Consider now that it is the goal of the National Cholesterol Education Program to lower the intake of animal fat of all Americans to about ten per cent of their caloric intake. Almost fifteen per cent of the Tecumseh participants (42) already ate that little animal fat, and yet it was impossible to see a difference between the cholesterol of those who ate that little and of those who ate much more. Does it make sense to recommend this drastic reduction of animal fat intake if the cholesterol of those who already eat that little is just as high as the cholesterol of the others?

In the study from the Mayo Clinic (43) there was also a wide range of fat intake. The lowest intake of animal fat was 15 grams per day (less than 10 per cent of the caloric intake); the highest was 60 grams per day. In the Bogalusa study, the range was still broader. The lowest intake of all fats (no information was given about the range of intake of animal fat) was 17 grams per day, the highest 325 grams per day.

In Jerusalem a team of researchers, led by Dr. Harold Kahn studied the diet and blood cholesterol of ten thousand male Israeli civil servants. The dietary habits varied considerably between people coming from Israel, Eastern Europe, Central Europe, Southern Europe, Asia and Africa. The intake of animal fat varied from ten grams up to two hundred grams daily, and there were also considerable differences between their cholesterol values (47).

If the intake of animal fat were of major importance for the cholesterol level in the blood it should be possible to find some kind of relationship from a study of so many individuals with such great variations in blood cholesterol and dietary habits. But there was no relation in this Israeli study either. Extremely low cholesterol values were seen both in those who ate little and in those who ate the most animal fat, and high cholesterol values were seen at all levels of animal fat intake.

The scientists from Israel also studied the value of various ways of dietary questioning. Many studies have recorded the diet of a 24 hour period only. Even if this information were accurate it may not be representative of the diet for the rest of the year, far less for a whole life time. The Israeli scientists found that the best information came from a questioning over several days in different seasons of the year, the method used in the study of the bank staff members. Using this expensive and time-consuming method in a smaller study of sixty-two individuals they could not find a correlation either; the correlation coefficient between animal fat intake and blood cholesterol was zero point zero (48).

Vegetarians usually have lower cholesterol than other people and they eat little animal fat. But vegetarians differ from the rest of the human population in more than their diet. They usually smoke less, they are usually thinner, and they usually exercise more often than other people. Whether it is their diet, or their other living habits, or perhaps something else that lowers their blood cholesterol is unknown.

The fact that blood cholesterol is influenced by the diet in laboratory experiments and clinical trials but not in people who live without the interference of scientists and dieticians has a simple explanation: blood cholesterol is controlled by more powerful factors than the diet. If these factors are kept reasonably constant in a laboratory experiment or a clinical trial, it is possible to see the influence of the diet alone.

The question is, however, if a lowering of blood cholesterol by diet is permanent. As mentioned above, the body tends to keep its blood cholesterol at about the same level. The dietary experiments mentioned above went on for a few months at most. The cholesterol control of the human body probably needs more time to adapt to a fat intake that differs from the usual one. Over millions of years mammals and their latest contribution, homo sapiens (our kind of men), have developed effective mechanisms to counteract unfavorable changes of all blood constituents. Salt and water, for instance, are regulated rapidly within narrow limits, because even small deviations may have a strong influence on the functions of the body. Extreme variations of other substances, such as proteins and fats, have no serious consequences in the short run; the adaptation is thus slow. But in due time also these deviations may be counteracted; this has been demonstrated by the Masais, the Samburus, the Somalian shepherds, and many others.

And even if blood cholesterol should become temporarily elevated because we eat great amounts of animal fat, a high cholesterol is not necessarily dangerous to the heart (see [section 1](#)).

#### **4. Atherosclerosis and coronary heart disease have nothing to do with the diet**

National consensus committees in many countries have declared that atherosclerosis and coronary heart disease can be prevented by an appropriate diet. Although the scientific evidence for this message is surprisingly meager, if present at all, it has gained status as established wisdom.

The definition of the "prudent" diet has changed considerably with time. Initially, it was considered important to reduce dietary fat of all kinds. This advice was based on a review paper by Ancel Keys (49), the main designer of the so-called diet-heart idea. In his review Keys presented a perfect curvilinear correlation between the mortality from coronary heart disease and the consumption of fat in six countries, but his curve was based on a selection of countries that fit his hypothesis and it has not been confirmed in studies including many more countries (50).

The prudent diet was redefined a few years later based on a new study by Ancel Keys, "Seven Countries" (51). According to that study the total fat intake was unimportant; heart mortality in these seven countries was best predicted by the intake of *saturated* fat . But *within* each country no association was seen. In Finland and Greece for instance, heart mortality in two districts varied with a factor five and seven, respectively, despite similar diets and other risk factors. Furthermore, no correlation was found between the diet and the major electrocardiographic findings. Considering that all electrocardiograms were analysed in the American study center this finding should carry more weight than the correlation with the clinical diagnosis, settled as it was by local doctors with varying competence and diagnostic habits.

The seven countries were admittedly selected by Keys. Such selection may be helpful to illustrate an idea at a preliminary stage, but a proof of causality demands random data. In more recent studies, including many more countries, the association was weak, absent, or inverse (52).

Conclusions from associations between national food consumption data and disease should be drawn with care. Most important, assumed intake of animal fat may be falsely high in prosperous countries, because available fat is not the same as fat eaten, but includes fat consumed by pet animals, fat discarded in the kitchen or on the plate, and fat which has never reached the consumer. With all certainty, these amounts are larger in prosperous countries.

The finding that an increased intake of polyunsaturated fatty acids, also called PUFA, can lower the serum cholesterol concentration in laboratory experiments has led to the belief that they would lower the risk of coronary heart disease also. Consequently, an increased intake of PUFA has been advised as an important part of the prudent diet. Initially, no limit was put to such intake, but by the years the limit has been lowered successively. Most recently, an upper limit of only 7 cal% was recommended because a high intake of PUFA promotes cancer, infections and testicular damage in rats (53). The average food intake in most western countries includes that amount of PUFA.

There is little evidence that an increased intake of PUFA protects against heart attacks. In "Seven Countries" intake of PUFA was not associated with heart mortality, and studies of patients with coronary heart disease have shown that if anything, they eat *more* PUFA than do healthy individuals, see below.

If heart attacks are caused by eating too much animal fat or saturated fat, a rising intake in a population should of course be followed by more heart attacks and a decreasing intake by fewer attacks. No consistent pattern has been found, however. In a few countries the changes have followed each other and the data from these countries have been used eagerly to support national diet counseling. But in many countries fat consumption has changed whereas heart mortality has not, or *vice versa*; in many countries they have even changed at opposite directions (54).

In Switzerland, for instance, coronary mortality decreased after World War II. During the same period intake of animal fat increased by 20 per cent (55).

In England, the intake of animal fat has been relatively stable since at least 1910 while the number of heart attacks increased ten times between 1930 and 1970 (56).

In the US coronary mortality increased about ten times between 1930 and 1960, leveled off during the sixties and has since decreased. During the decline of mortality from coronary heart disease the consumption of animal fat declined, but so it did during the previous thirty years of sharply rising mortality (57). In Framingham the decline of coronary mortality was balanced by

an increased number of non-fatal heart attacks (58) suggesting an effect of better treatment rather than an effect of dietary changes.

In Japan coronary heart disease is uncommon, allegedly due to the lean Japanese diet. A large study of Japanese emigrants (59) is often used as evidence because after migration to the United States these emigrants died from heart attacks almost as often as did Americans. The increased heart mortality after migration was not associated with the diet or the serum cholesterol, however, but with the cultural upbringing; those who lived according to Japanese traditions were protected. Most surprising, emigrants who stuck to the Japanese tradition, but ate the fat American food ran a smaller risk than those who were accustomed to the American way of life but ate the lean Japanese food (60).

If dietary fats were important this should obviously be reflected in the diet of patients who have had a heart attack. The following table gives the results from 13 studies, where the diet of patients with coronary heart disease was compared with the diet of healthy control individuals of the same age and sex. The amounts of dietary fats are given in percent of total calories. Asterisks means that the difference found was statistically significant. NS means that no absolute figures were given in the report, but that the difference was not statistically significant.

Main Author	Population	Saturated fatty acids		Poly-unsaturated fatty acids	
		Patients with heart disease	Healthy control individuals	Patients with heart disease	Healthy control individuals
Paul (61)		17.2	16.7	3.9	4.0
Medalie (62)		NS	NS	NS	NS
Yano (63)		13	12	7	6
Garcia-Palmieri (64)	urban	13.6	13.5	6.7**	5.9
	rural	13.1	12.6	3.9	3.9
Gordon (65)	Framingham	15.3	14.9	5.8	5.4
	Puerto Rico	13.5	13.3	6.0**	5.3
	Honolulu	12.7	12.3	6.7**	6.0
McGee (66)		12.7*	12.3	6.3*	6.0
Kromhout (67)		17.7	17.6	5.9	5.9
Kushi (68)		17.4	16.9	2.6	2.7
Khaw (69)	men	13.6	13.7	6.7	6.6
	women	13.1	13.8	7.2	6.9
Posner (70)	45-55 years	NS	NS	NS	NS
	55-65 years	NS	NS	NS	NS
Zuckel (71)		18.7	18.9	3.6	3.6
Finegan (72)		19	18	4	4

<b>Bassett (73)</b>	Hawaiian men	13.3	13.2	5.4	5.9
	Japanese men	10.7	11.1	6.3	6.3

As you see, the differences were very small and in most cases due to chance. In only one study patients ate more saturated fatty acids than did healthy controls, but in the same study and in a further three, patients ate more *polyunsaturated* fatty acids, contrary to what was predicted from the message we have heard for so many years.

The prudent diet is thought to operate by lowering serum cholesterol and a low serum cholesterol is thought to prevent premature atherosclerosis. Logically, degree of atherosclerosis at autopsy should reflect the diet, but again, findings are contradictory.

In the "Geographic study", which included more than 21000 autopsies in 14 countries (74) degree of atherosclerosis in each country was associated with the total intake of fat in that country, but not with intake of fat of animal origin indicating that the total amount of fat, or the amount of vegetable fat should be decisive.

Japan was not included in that study, however. In comparative autopsy studies at a time where the intake of all fats and also animal fat was about three times larger in the US than in Japan, degree of atherosclerosis was similar in these two populations (35,36). Thus, if Japan had been included in the Geographic study the mentioned correlation with all certainty should have disappeared.

It may be argued that information about the diet in these studies was collected from the literature and may not have reflected the individual intake of those who participated in the study, but no association was found either in smaller studies that included an assessment of each individual's diet (75).

The crucial test is the controlled, randomised trial. Eight such trials using diet as the only treatment has been performed (76), but neither the number of fatal or non-fatal heart attacks were reduced significantly in any of these trials, not even if the results were added in a meta-analysis. A recent, small trial, which included the addition of alfa-linolenic acid to the diet, was succesful (77), but in that trial the serum cholesterol concentration was unaltered by the diet leaving us with more questions than answers.

## 5. Cholesterol-lowering may shorten your life

According to conventional wisdom it is wise to lower your cholesterol if it is too high. The main reason for this advice is the observation that people with a high cholesterol more often get a heart attack than people with a normal or a low cholesterol. The observation is correct, but it does not mean that the high cholesterol is the cause of the heart attack (see section 1). If it were, lowering of the high cholesterol by any means should prevent it, but it doesn't (except with the new group of cholesterol-lowering drugs, the statins; see below).

More than 40 trials have been performed to test if cholesterol-lowering can prevent a heart attack. In some of the trials the number of fatal heart attacks were lowered a little, in other trials the number of fatal heart attacks increased. Overviews of the trials have shown that when all results were taken together, just as many died in the treatment groups (e.g. those whose cholesterol was lowered) as in the untreated control group (78,79). The following table gives the accumulated results. None of the differences were statistically significant. Nor were they by more sophisticated analyses.

	<b>Treatment groups</b>	<b>Control groups</b>
<b>Number of individuals on trial</b> <b>Non-fatal heart attacks; per cent</b>	<b>59,514</b> <b>2.8</b>	<b>53,251</b> <b>3.1</b>
<b>Number of individuals on trial</b> <b>Fatal heart attacks; per cent</b>	<b>60,824</b> <b>2.9</b>	<b>54,403</b> <b>2.9</b>
<b>Number of individuals on trial</b> <b>Total number of deaths; per cent</b>	<b>60,456</b> <b>6.1</b>	<b>53,958</b> <b>5.8</b>

That some overviews have shown a positive result after cholesterol-lowering is because they had ignored or excluded one or more trials with a negative outcome [\(79\)](#).

The mentioned overviews included mostly diet and/or the older cholesterol-lowering drugs. But a new type of drugs, the so-called statins (for instance Zocord®, Mevacor®, Lescol®, Lipitor® and Pravachol®) have been successful. However, their effect isn't exerted through cholesterol-lowering, they have other and more useful properties. Unfortunately they also stimulate cancer growth (see [section 6](#)).

## **6. The effect of the statins is not due to cholesterol-lowering**

As mentioned in [section 4](#) cholesterol-lowering by itself does not prolong your life. In the experiments, that have shown this fact beyond all doubt, cholesterol-lowering was performed by diet or by use of various older drugs such as clofibrate (Atromidin®), gemfibrozil (Lopid®), cholestyramine (Questran®), colestipol (Lestid®), and nicotinic acid (Nicangin®).

But a new type of cholesterol-lowering drugs, the so-called statins (for instance Zocord® and Pravachol®) have been successful. For the first time cholesterol-lowering have shown significant improvement of mortality, both coronary mortality, stroke mortality and total mortality. These trials are therefore considered as strong arguments for the idea, that a high cholesterol is dangerous.

Have these trials really demonstrated that raised LDL cholesterol has importance for coronary heart disease, as the trial directors concluded in the reports?

There is reason to question that, because some of the results are not consistent with what we have learned about cholesterol.

First, old patients were protected from cardiovascular disease just as much (or as little) as young ones, although most studies have shown that a high cholesterol is a weak risk factor, or no risk factor at all, for old people. (Unfortunately, in the only trial that included old people only, the PROSPER trial, the lowering of heart mortality was smaller than the increase of cancer mortality).

Second, also the number of strokes was reduced after statin treatment, although no studies have shown that a high cholesterol is a risk factor for stroke.

Third, patients who had had a coronary were protected although most studies have shown that a high cholesterol is a weak risk factor, if any at all, for those who already have had a

coronary. (In fact, this finding should have stopped all the previous, secondary preventive trials).

And finally, the statins protected against coronary heart disease whether the cholesterol was high or low although most studies have shown that a normal or low cholesterol is no risk factor for coronary disease.

How come that the statins are effective for old people, for patients who already have had a coronary, and even for those whose cholesterol is normal? If the cholesterol level for these people is no risk factor for coronary disease, how could a lowering of that cholesterol improve their chances to avoid a coronary? The only reasonable explanation is that the statins do more than just lower cholesterol. There is much evidence for that.

The statins inhibit the body's production of a substance called mevalonate, which is a precursor of cholesterol. When the production of mevalonate goes down, less cholesterol is produced by the cells and thus blood cholesterol goes down as well. But mevalonate is a precursor of other substances also, substances with important biologic functions. The metabolic pathways are not known in all details, but less mevalonate may explain why simvastatin makes smooth muscle cells less active and platelets less inclined to produce thromboxane. One of the first steps in arteriosclerosis is the growth and migration of smooth muscle cells inside the artery walls; and thromboxane is a substance which promotes the clogging of blood. Thus, by blocking the function of smooth muscle cells and platelets, simvastatin may benefit cardiovascular disease by at least two mechanisms and both of these mechanisms are independent of the cholesterol level (82). In fact, up till now we have learned about eleven anti-atherosclerotic effects of statin treatment, that have been found independent on their effect on cholesterol

In one of the experiments for instance, performed by Dr. Yusuke Hidaka and his team, the inhibitory effect on the muscle cells could not be abolished by adding LDL-cholesterol to the test tubes (83); and in experiments with various cholesterol-lowering agents, thromboxane production was inhibited by statins only, indicating that the effect was not due to cholesterol lowering but to something else (82).

The protective effects of simvastatin was also demonstrated in animal experiments. In one of them, performed by Dr. B.M. Meiser and colleagues from Munich, Germany, hearts were transplanted into rats. Normally, the function of such grafts gradually deteriorates because the coronary vessels are narrowed by an increased growth of smooth muscle cells in the vascular walls, a condition called graft vessel disease. In Dr. Meiser's experiment, however, rats that were given simvastatin had considerably less graft vessel disease than control rats not given simvastatin, and this was not due to cholesterol lowering because simvastatin does not lower cholesterol in rats. In fact, LDL cholesterol was highest in the rats treated with simvastatin (84).

In another experiment, Dr. Maurizio Soma and his colleagues from Milan, Italy placed a flexible collar around one of the carotic arteries in rabbits. After two weeks arteries with collars became narrow but less so if the rabbit had been given simvastatin. Again, the effect was unrelated to the rabbits' cholesterol level (85).

Thus, the statins in some way protect against cardiovascular disease, but their effect is not due to cholesterol-lowering.

But why bother about pharmacological mechanisms? Isn't it wonderful that the statins work? Shouldn't we all take statins?

## **The costs**

To answer that question it is necessary to look at the figures from the trials. To be short I have chosen the figures for coronary death. According to the results from the 4S trial (86) there was a 41% reduction in the risk of coronary death. According to the results from the CARE trial (87) the reduction was 24%, and according to the WOSCOP (88) trial the reduction was 28%. These figures seem impressive, but let us look at the absolute figures also.

In the treatment group of the 4S trial five percent, or 111 individuals, died from a heart attack; in the control group 8.5 percent, or 189 individuals, died, a difference, or a risk reduction of 3.5%. To prevent these 3.5% of the patients (8.5% - 5%) or 78 individuals, from dying it was necessary to treat 2221 individuals during five years. You could also say that to prevent one death it was necessary to treat 25 individuals for five years. Or said in another way, if you have had a heart attack the chance to avoid death from a new one during five years is 91.5%. If you eat simvastatin this chance increases to 95%.

In the CARE trial 5.7%, or 119 individuals died from a heart attack in the control group and 4.6%, or 96 individuals in the treatment group. Thus, to prevent 23 coronary deaths (1.1%) it had been necessary to treat 2081 individuals for five years, which means that 90 patients were treated for each life saved.

In the WOSCOP trial, which concerned healthy individuals with a high cholesterol, the result was even less impressive. Here, 61 died in the placebo group, 41 in the treatment group, a risk reduction of 0.6%. To save these 20 lives it had been necessary to treat 3302 healthy individuals for five years, or 165 individuals for each life.

Said in another way, the risk of dying from a heart attack during five years if you are about 55 years old and if your cholesterol is around 272 mg per dl is 1.8%. With pravastatin treatment the risk is reduced to 1.2%. You could also say that the chance to avoid death from a heart attack for five years is 98.2%; with pravastatin the chance is 98.8%.

The reason why trial results should be given in absolute figures and not in relative is because the side effects are given in absolute figures. Let us assume that a mortal side effect occurs in 0.5 percent of the patients. You may belittle that if you compare this figure for instance with a relative risk reduction of 28%. But as the absolute risk reduction was 0.6% the effect of treatment has almost disappeared.

To be fair it should be mentioned that the number of non-fatal heart attacks was reduced also. In the WOSCOP trial for instance, 248 individuals in the control group had a fatal or non-fatal coronary, in the pravastatin group the number was 174. This means that to prevent a heart attack in a healthy 55 year old man with a high cholesterol it is necessary to treat about 45 men for five years. To prevent a new heart attack it is necessary to treat 34 patients for five years according to the CARE trial and 28 patients according to the 4S trial.

It is necessary also to look at the costs, but this is not an easy task. For the drugs only the price for one extra year for one person was about \$41,000 in the 4S trial, about \$148,000 in the CARE trial and about \$205,000 in the WOSCOP trial. To that should be added the costs for laboratory tests and doctors' fee.

There are economical gains also, of course. The directors of the most successful trial 4S claim that the reduced costs due to the lower number of non-fatal heart attacks outweigh the expenses. But that trial concerned patients at a very high risk of cardiovascular disease. To treat *healthy* individuals with a high cholesterol must be very expensive, however, because the gain was very small.

The 4S directors' optimistic views presuppose that the effect is just as positive after ten or twenty years of treatment as it was after five. Unfortunately we cannot guarantee that. Recently, Drs. Thomas Newman and Stephen Hulley published the results from a meticulous review of what we know about cancer and lipid-lowering drugs. They found that clofibrate, gemfibrozil and all the statins stimulate cancer growth in rodents [\(89\)](#).

Newman and Hulley asked themselves why these drugs had been approved by the Food and Drug Administration at all. The answer was that the doses used in the animal experiments were much higher than those recommended for clinical use. But as Drs. Newman and Hulley commented, it is more relevant to compare blood levels, and the levels achieved in rodents were very close to those seen in patients.

Because the latent period between exposure to a cancer-stimulating chemical and the incidence of clinical cancer in humans may be 20 years or more, the absence of any controlled trials of this duration means that we do not know whether statin treatment will lead to an increased rate of cancer in coming decades. There is reason to believe that it will, because as mentioned above, treatment of old people already has resulted in an increased number of cancer. The reason is probably that many old people already have cellular changes that rapidly may develop to clinical cancer if stimulated by a cancer-provoking drug..

Other nasty effects have been reported on human beings, side effects that have been reported after the end of the trials. They include peripheral neuropathy, a painful and invalidating disease mainly located to the legs [\(90a\)](#), memory loss [\(90b\)](#), short temper [\(90c\)](#), aggressive behavior [\(90d\)](#) and muscle problem that in rare cases have led to kidney failure and death. Most scary, considering that people with very high cholesterol, so-called familial hypercholesterolemia, automatically are prescribed statin treatment already from early childhood, is the recent report in prestigious New England Journal of Medicine [\(90e\)](#). Here the authors reported that almost 50 % of pregnant women who took a statin drug during early pregnancy gave birth to a child with malformations, some of them more severe than those seen after thalidomide treatment.

Those who argue for statin treatment have argued that these side effects are very rare. They will most certainly become much more common considering that the new cholesterol guidelines recommend that cholesterol should be lowered as much as possible, even if it may demand an eight times higher dose than used hitherto.

Thus, millions of asymptomatic people are being treated with medications, the ultimate effects of which are not yet known. Drs. Newman and Hulley therefore recommended that the new statins should be used for patients at very high risk for coronary disease only, whereas such treatment should be avoided for individuals with life expectancies of more than 10 to 20 years. And healthy people with a high cholesterol as the only risk marker belong to that category.

## 7. The many critical scientists

Those who propagate for a low-fat diet and cholesterol-lowering drugs claim that there is general agreement about the diet-heart idea. Nothing could be more wrong. Here follows, in alphabetic order, a selection of critical scientists.

**Mary Enig** is an international expert in the field of lipid biochemistry, a nutritionist and a Consulting Editor to a number of scientific publications, among others the Journal of the American College of Nutrition. She is also the President of the Maryland Nutritionists Association. She has published many scientific papers on the subject of food, nutrition topics, food fats and oils, several chapters on nutrition for books and a book about dietary fats, oils and cholesterol [\(90a\)](#). Her main research has concerned the hazards associated with eating too

much trans fatty acids. In an interview she was asked if saturated fats cause heart disease: *The idea that saturated fats cause heart disease is completely wrong, but the statement has been "published" so many times over the last three or more decades that it is very difficult to convince people otherwise unless they are willing to take the time to read and learn what all the economic and political factors were that produced the anti-saturated fat agenda.* Read also hers and Sally Fallons paper [The Oiling of America](#)

**Michael Gurr** is an associate professor of biochemistry at the School of Biological & Molecular Sciences in Oxford, editor-in-chief of *Nutrition Research Reviews* and editor of three other scientific journals. Wrote Professor Gurr in his conclusion of a large review on the diet-heart idea [\(91\)](#): *The arguments and discussion of the scientific evidence presented in this review will not convince those "experts" who have already made up their minds, for whatever reason, be it truly scientific or political, that a fatty diet is the cause of CHD [coronary heart disease]. However, I hope that some readers, who were, perhaps, unaware that the lipid hypothesis had any shortcomings, will have been persuaded that the relationships between the fats we eat and the likelihood that we may die from a heart attack is by no means as simple as these simplistic statements imply.*

**George Mann**, now retired, was previously a professor in medicine and biochemistry at Vanderbilt University in Tennessee. From his studies of the Masai people (see [section 3](#)) he realized that diet couldn't possibly be the main cause of high cholesterol and coronary heart disease. As long ago as 1977, in *The New England Journal of Medicine* he published a strong argument against the diet-heart idea citing the lack of relationship between dietary habits and blood cholesterol, the lack of correlation between this century's trends in fat consumption and death rates in the United States, and the disappointing outcome of the cholesterol lowering trials [\(92\)](#).

After the start of the cholesterol campaign eight years later Mann summarized his criticism of the diet-heart idea in *Nutrition Today* [\(93\)](#). According to Mann, the diet-heart idea is *the greatest scientific deception of our times*. Mann is especially critical of the cholesterol-lowering trials. *Never in the history of science have so many costly experiments failed so consistently*, he declared.

Professor Mann also criticized the directors of the Lipid Research Clinics trial (LRC), the fundament of the cholesterol campaign. The unsupportive results from the LRC trial have not prevented them from *bragging about this cataclysmic break-through*, he wrote. And, he continued: *The managers at the National Institutes of Health have used Madison Avenue hype to sell this failed trial in the way the media people sell an underarm deodorant. The Bethesda Consensus Panel ... has failed to acknowledge that the LRC trial, like so many before it, is saying firmly and loudly 'No, the diet you used is not an effective way to manage cholesterolemia or prevent coronary heart disease and the drug you so generously tested for a pharmaceutical house does not work either.*

People who are faced with the many distorted facts about diet, cholesterol and heart disease often ask me why so many scientists unquestioningly accept the diet-heart idea. Here is Professor Mann's comment: *Fearing to lose their soft money funding, the academicians who should speak up and stop this wasteful anti science are strangely quiet. Their silence has delayed a solution for coronary heart disease by a generation.*

Professor Mann offers a little glimpse of hope at the end of his article in *Nutrition Today* [\(93\)](#): *Those who manipulate data do not appreciate that understanding the nature of things cannot be permanently distorted - the true explanations cannot be permanently ignored. Inexorably, truth is revealed and deception is exposed. ... In due time truth will come out. This is the relieving grace in this sorry sequence.*

**Michael F. Oliver**, a former professor and director of the Wynn Institute for Metabolic Research, London was one of the first to demonstrate that, on average, patients with coronary heart disease more often had abnormal levels of various fats in the blood than control individuals did. Professor Oliver still thinks that those with inherited diseases of cholesterol metabolism, or those at a very high risk for cardiovascular risk may benefit from cholesterol lowering, but in several papers he has warned against campaigns for cholesterol lowering in the general population: *Doubts about the promotional nature of these campaigns are not popular. Doubters are scorned, although this does not matter. But the issue is a very serious one if vast sums are spent and widespread changes are made in the lifestyle of normal people when the accumulated evidence is that total mortality is unchanged or possibly even increased* (94).

Again and again, Professor Oliver has criticized those who think that the increased mortality from non-medical causes seen in many trials is an effect of chance. Rather, he thinks, the very lowering of blood cholesterol may be dangerous: *Very little is known about the long-term effects of lowering cholesterol concentrations on the composition of cell membranes* (95).

According to Oliver our bodies may regulate attempts to lower blood cholesterol in most cases, but *...would such homoeostatic [regulatory] mechanisms be effective in all patients, at all times, and in all cells--particular cells in which biologic function is impaired for other reasons? These doubts will not go away for several more years?* (95)

#### [Other critical papers by Professor Oliver](#)

**Edward R. Pinckney** is an editor of four medical journals and former co-editor of *JAMA*, the *Journal of the American Medical Association*. In 1973, together with his wife, he published a book, called "The Cholesterol Controversy" (97) which summarized all the inconsistencies of the cholesterol idea. Dr. Pinckney describes all the factors that influence blood cholesterol in healthy people and how difficult it is to get a reliable measure of the cholesterol level because of the uncertainties of the analysis: *The level of one's blood cholesterol is, at best, nothing more than an extremely rough indication of a great many different disease conditions. At worst, it can be more the cause of stress and the diseases that stress brings on. To alter one's life style as a consequence of this particular laboratory test may well cause more trouble than it could relieve.*

The start of chapter 1 in Pinckney's book is worth citing: *Your fear of dying--if you happen to be one of the great many people who suffer from this morbid preoccupation- may well have made you a victim of the cholesterol controversy. For, if you have come to believe that you can ward off death from heart disease by altering the amount of cholesterol in your blood, whether by diet or by drugs, you are following a regime that still has no basis in fact. Rather, you as a consumer, have been taken in by certain commercial interests and health groups who are more interested in your money than your life.*

**Raymond Reiser** is a former professor of biochemistry at Texas A&M university. In 1973 he criticized the recommendations for dietary treatment of high cholesterol by declaring: *The authority quoted by these authors for the recommendation is not a primary source but another review similar to their own. It is this practice of referring to secondary or tertiary sources, each taking the last on faith, which has led to the matter-of-fact acceptance of a phenomenon that may not exist.* (98)

Here is another citation from Professor Reiser's papers (99): *One must be bold indeed to attempt to persuade large segments of the populations of the world to change their accustomed diets and to threaten important branches of agriculture and agribusiness with the results of such uncontrolled, primitive, trial and error type explorations. Certainly modern science is capable of better research when so much is at stake.*

**Paul Rosch** is President of The American Institute of Stress, Clinical Professor of Medicine and Psychiatry at New York Medical College, Honorary Vice President of the International Stress Management Association and Chairman of its U.S. branch. He is the editor or subeditor of three well-known medical journals, he has been a member of the board of several other journals, and has served as President of the New York State Society of Internal Medicine, as Chairman of the International Foundation for Biopsychosocial Development and Human Health, and has been an Expert Consultant on Stress to the United States Center for Disease Control. He has written extensively over the past forty-five years on the role of stress in health and illness, with particular reference to cardiovascular disease and cancer. He has appeared on numerous national and international television programs such as The Today Show, Good Morning America, 60 Minutes, Nova, CBS, NBC, PBS, BBC and CBC network presentations. His editorials and comments have been published in every major medical journal. Professor Rosch has also been interviewed and widely quoted in numerous major American newspapers and magazines.

As the author of the Newsletter of the American Institute of Stress Professor Rosch has published several articles about the cholesterol hypothesis and the diet-heart idea. His conclusions are close to those presented in this book: *A massive crusade has been conceived to "lower your cholesterol count" by rigidly restricting dietary fat, coupled with aggressive drug treatment. Much of the impetus for this comes from speculation, rather than any solid scientific proof.*"

The result is well-known, says Professor Rosch: *The public is so brainwashed, that many people believe that the lower your cholesterol, the healthier you will be or the longer you will live. Nothing could be further from the truth.*

How can this go on year after year? Professor Rosch has several explanations: *The cholesterol cartel of drug companies, manufacturers of low fat foods, blood testing devices, and others with huge vested financial interests have waged a highly successful promotional campaign. Their power is so great that they have infiltrated medical and governmental regulatory agencies that would normally protect us from such unsubstantiated dogma.*

Professor Rosch reminds us that practicing physicians get most of their information from the drug companies. But compared to their peers a half century ago, most doctors don't have the time or skills to critically evaluate reports, very few know anything about research, nor did the generation that taught them.

**Ray Rosenman** is the retired Director of Cardiovascular Research in the Health Sciences Program at SRI International in Menlo Park, California, and associate chief of medicine, Mt Zion Hospital and Medical Center in San Francisco. Since 1950 he has been a cardiologist and a researcher. He has published four books and many text chapters and journal articles about cardiovascular diseases. His main interest has been the influence of neurogenic and psychological factors on the blood lipids [\(100\)](#), but he has also written reviews critical of the diet-heart idea.

Here is the conclusion from his most recent review: *These data lead to a conclusion that neither diet, serum lipids, or their changes can explain wide national and regional differences of IHD [coronary heart disease] rates, or the variable 20th century rises and declines of CHD mortality. This conclusion is supported by the results of many clinical trials which fail to provide adequate evidence that lowering serum cholesterol, particularly by dietary changes, is associated with a significant reduction of IHD mortality or improved longevity. It is variously stated that the preventive effects of dietary and drug treatments have been exaggerated by a tendency in trial reports, reviews, and other papers to cite and inflate supportive results, while suppressing discordant data, and many such examples are cited [\(101\)](#).*

**Russell Smith** was an American experimental psychologist with a strong background in physiology, mathematics and engineering. No review written by the proponents of the diet-heart idea are remotely comparable with Smith's books and papers [\(102\)](#) when it comes to scientific depth and completeness. Smith's summation is devastating for the diet-heart proponents: *Although the public generally perceives medical research as the highest order of precision, much of the epidemiologic research is, in fact, rather imprecise and understandably so because it has been conducted principally by individuals with no formal education and little on-the-job training in the scientific method. Consequently, studies are often poorly designed and data are often inappropriately analyzed and interpreted. Moreover, biases are so commonplace, they appear to be the rule, rather than the exception. It is virtually impossible not to recognize that many researchers routinely manipulate and/or interpret their data to fit preconceived hypotheses, rather than manipulate hypotheses to fit their data. Much of the literature, therefore, is nothing less than an affront to the discipline of science.*

Dr. Smith concludes: *The current campaign to convince every American to change his or her diet and, in many cases, to initiate drug "therapy" for life is based on fabrications, erroneous interpretations and/or gross exaggerations of findings and, very importantly, the ignoring of massive amounts of unsupportive data...It does not seem possible that objective scientists without vested interests could ever interpret the literature as supportive.*

Dr. Smith is aware that he is up against some extremely powerful institutions: *The political and financial power of the NHLBI and AHA team...is enormous and without equal. And because the alliance has substantial credibility in the eyes of the public and most practicing physicians, it has become a juggernaut, able to use its power and prestige to suppress a great body of unsupportive evidence and even defy the most fundamental tool of scientists, logic.*

The scientists who have produced the misleading papers and reviews are, of course, the first whom Smith faults. But he adds: *Equally culpable are the editors of the many journals who publish articles without regard to their quality or scientific import. It is depressing to know that billions of dollars and a highly sophisticated medical research system are being wasted chasing windmills.*

**William E. Stehbens** is a professor at the Department of Pathology, Wellington School of Medicine, and director of the Malaghan Institute of Medical Research in Wellington, New Zealand. Based on his own studies and on extensive reviews of the literature he has effectively demonstrated the many fallacies of the diet heart-idea. In a thorough review of the experimental studies he concluded: *Upon examination of this evidence and consideration of the specific criteria for the experimental production of atherosclerosis, any pathologist of independent mind and free from preconceived ideas would conclude that human atherosclerosis and the lesions induced by the dietary overload of cholesterol and fats are not one and the same disease [\(103\)](#).*

Professor Stehbens has also pointed out the weaknesses of the epidemiologic studies that have used mortality statistics as proof for causality: *Continued, unquestioned use of unreliable data has led to premature conclusions and the sacrifice of truth. The degree of inaccuracy of vital statistics for CHD is of such uncertain magnitude that, when superimposed on other deficiencies already indicated, the concept of an epidemic rise and decline of CHD in many countries must be regarded as unproven, and governmental or health policies based on unreliable data become untenable [\(104\)](#).*

According to Professor Stehbens atherosclerosis is due to wear and tear of the arteries, not to too much cholesterol in the blood, and he has many good arguments for this idea. The following words from a 1988 paper [\(105\)](#) summarize Stehbens' view on the diet-heart idea: *The perpetuation of the cholesterol myth and the alleged preventive measures are doing the dairy and meat industries of this and other countries much harm quite apart from their*

*potential to endanger optimum nutrition levels and the health of the populace at large...It is essential to adhere to hard scientific facts and logic. Scientific evidence for the role of dietary fat and hypercholesterolemia in the causation of atherosclerosis is seriously lacking...The lipid hypothesis has enjoyed undeserved longevity and respectability. Readers should be aware of the unscientific nature of claims used to support it and see it as little more than a pernicious bum steer.*

[Other critical papers by Professor Stehbens](#)

**Lars Werkö**; now retired, was previously a professor of medicine at Sahlgren's Hospital, Gothenburg, Sweden, when he moved to become scientific director at the Astra Compagny. Later on he became head of the Swedish Council on Technology Assessment in Health Care, a governmental agency. Professor Werkö has been an opponent of diet-heart for many years. In 1976 he criticized the design in the large epidemiologic studies aimed at preventing coronary heart disease, most of all the Framingham study.

According to Professor Werkö [\(107\)](#) the dogm is based on questionable "facts" rooted in hopes, wishful thinking and studies using selected materials: *No studies have proved anything, but instead of formulating new hypotheses diet-heart supporters call the current one the most probable truth, and they have intervened in people's lives because they will not wait for the final proof.*

[Other critical papers by Professor Werkö](#)

**These were some of the most important critics, but there are many more. Go to [THINCS](#), The International Network of Cholesterol Skeptics**

## 8. How to create a false idea

In the numerous reviews written by upholders of the diet-heart idea it is often said that this idea is based on "strong, scientific data", the evidence is "overwhelming" or "extremely powerful" and "controversy is unjustified". If you have read the previous sections you will understand that nothing could be more advanced from the truth. To use such vocabulary it has been necessary to exaggerate trivial, apparently supportive findings, to belittle or ignore the wealth of controversial and disproving evidence and to quote unsupportive results as if they were supportive.

How a "fact" is created by misquoting unsupportive findings and exaggerating trivial findings is exemplified in [section 1](#), the story about the so-called "good" and "bad" cholesterol.

Observations that are totally devastating for the diet-heart idea are mostly ignored. A good example is the fact that if we exclude individuals with the rare disease familial hypercholesterolemia (less than 0.5 percent of mankind suffer from it) there is no association between the level of blood cholesterol and the degree of vascular atherosclerosis ([section 2](#)).

Another one. Before the statin-era overviews of all cholesterol-lowering trials have shown that mortality cannot be improved by lowering cholesterol. But diet-heart proponents usually mention the trials with a positive outcome only and ignore the trials with a negative outcome.

**Thus, in 16 trial reports published between 1970 and 1992 a total of 40 citations were to (apparently) supportive or inconclusive trials, but with one exception, not a single citation was to unresponsive trials, although the number of supportive and unresponsive trials were equal (79).**

It is interesting to compare the number of citations of papers published in the same journal because few citations of a paper may simply reflect that it has been published in a little-known or less reputable journal. In 1984 The Lipid Research Clinic's coronary primary prevention trial was published in JAMA (110). In that trial 32 of the patients whose cholesterol was lowered died from a heart attack against 44 of the patients in the untreated control group. The total number of deaths (deaths from all causes) was 68 treated patients against 71 patients in the control group. These figures were not statistically significant by conventional statistics, but in spite of that the result was used as the main argument by the American cholesterol campaign.

In 1985 Dr. Miettinen and colleagues from Helsinki, Finland published another, but smaller cholesterol-lowering trial in the same journal (111). In that trial four patients whose cholesterol was lowered died from a heart attack, whereas only one died in the untreated control group, and the total number of deaths was ten in the treatment group against five in the control group.

Thus, both papers dealt with the same subject and were published in the same journal and no one has questioned the honesty of the experimenters or the quality of the studies. Reasonably, they should have been cited almost equally often. That the LRC trial, at least according to its directors, was supportive, and the Miettinen trial was not, is unimportant because the aim of research is to find the truth, whether it is happy or not. Here you can see how often the two papers have been cited by other scientists during the first four years after their publication:

	<b>Miettinen and co-workers</b>	<b>LRC-study</b>
<b>First year</b>	<b>6</b>	<b>109</b>
<b>Second year</b>	<b>5</b>	<b>121</b>
<b>Third year</b>	<b>3</b>	<b>202</b>
<b>Fourth year</b>	<b>1</b>	<b>180</b>

(Data according to Science Citation Index)

Needless to say, the paper by Miettinen has been cited mainly by more critical scientists.

An example of an unresponsive study which has been cited, many, many times, as if it was supportive is the Japanese migrant study. In Japan coronary heart disease is uncommon, allegedly due to the lean Japanese diet. A large study of Japanese emigrants (112) is often used as evidence because after migration to the United States, where the food generally is much fatter than in Japan, the serum cholesterol of these emigrants increased and they died from heart attacks almost as often as did Americans. The increased coronary mortality after migration was not associated with the diet or the serum cholesterol, however, but with the

cultural upbringing: those who lived according to Japanese traditions were protected against heart attacks.

**Especially striking was the finding that emigrants who stuck to the Japanese tradition, but ate American food ran a smaller risk of heart disease than emigrants who were accustomed to the American way of life but ate Japanese food [\(113\)](#).**

Here is another example. A common message from the American Heart Association and The National Heart, Lung, and Blood Institute to doctors is that there exist a close correspondence between degree of cholesterol lowering and degree of mortality reduction. Listen for example to the words from The Cholesterol Facts [\(114\)](#): "The results of the Framingham study indicate that a 1% reduction of cholesterol corresponds to a 2% reduction in CHD (coronary heart disease) risk." This statement was followed by a reference to a paper which reported the 30 years experience from Framingham [\(115\)](#).

But in that paper you can read the following statement:

**"For each 1 mg/dl drop of cholesterol there was an 11% increase (!) in coronary and total mortality."**

**The above examples are just the tip of the iceberg. Here is a systematic review of the way the three largest, authoritative reviews have misquoted the literature:**

Ravnskov U. [Quotation bias in reviews of the diet-heart idea](#). J Clin Epidemiol 1995; 48: 713-9.

**More recent examples of false citations are given in the following papers:**

Ravnskov U, Allan C, Atrens D, Enig MG, Groves B, Kaufman J, Kroneld R, Rosch PJ, Rosenman R, Werkö L, Nielsen JV, Wilske J, Worm N. [Studies of dietary fat and heart disease](#). Science 2002; 295:1464-1465.

Ravnskov U. [The diet-heart idea is kept alive by selective citation](#) Rapid Response BMJ 8. Dec 2003