«Healthy» diet and cholesterol screening to prevent coronary heart disease - An illustration of follies and fallacies in medicine

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The first part will digress into some general problems with health data and spurious statistics and the mechanisms surrounding the cholesterol scare. The second part looks into the question of cholesterol as a risk factor for coronary heart disease in some detail and into the question of whether changing the diet will change the burden of mortality. It is concluded that the promotion of cholesterol as an evil to whole nations and putting everyone on a «correct» diet is scientifically unjustified, medically foolish and politically ominous.

For centuries, it has been observed that people who eat, die. On the other hand, unfortunately, people who do not eat also die.

Experts have made the world believe that one perhaps could focus on a narrow area to find what is in the diet that causes people to die. You will always find experts who will provide an answer. So if you do not know you can always ask the experts.

Currently, coronary heart disease is the most common cause of death. Rather than admitting that we know very little about the etiology of coronary heart disease, the experts have provided seemingly definite answers. One such answer it that cholesterol is one of the major causes of coronary heart disease. In the first part, this contribution will digress into some relevant, general problems with health data and the mechanisms surrounding what nearly amounts to mass hysteria concerning the cholesterol scare, and in the second part, the question of cholesterol as a risk factor for coronary heart disease is examined in some detail.

[+] Editor's note: Due to his untimely death, Dr. Skrabanek was unable to finalize this manuscript himself. It has been rewritten posthumously by Richard E. Steele and Johannes G. Schmidt.

What can statistics show?

In *Fig. 1*, mortality rates for coronary heart disease in European countries are graphed. As one can see, it varies a great deal.

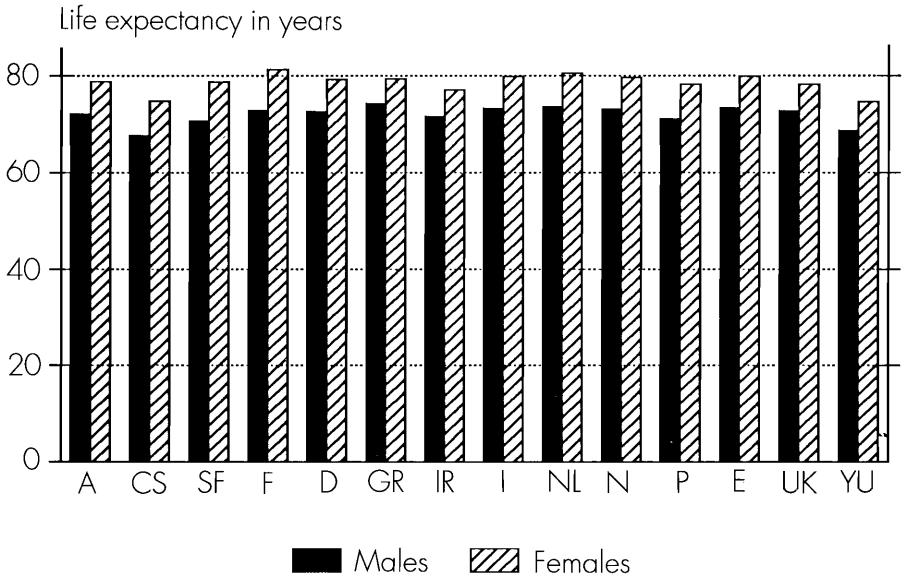
Fig. 1: Coronary heart disease mortality in 14 European countries

The *Mediterranean countries* (Portugal, Spain, France, Italy and Greece) have lower mortality rates than the northern European countries. The experts decided that surely there is a lesson to be learnt here, namely: If you eat the so-called *Mediterranean diet*, there is less chance of you dying of coronary heart disease.

Meanwhile, life expectancy *(Fig. 2)* is roughly the same in these countries.

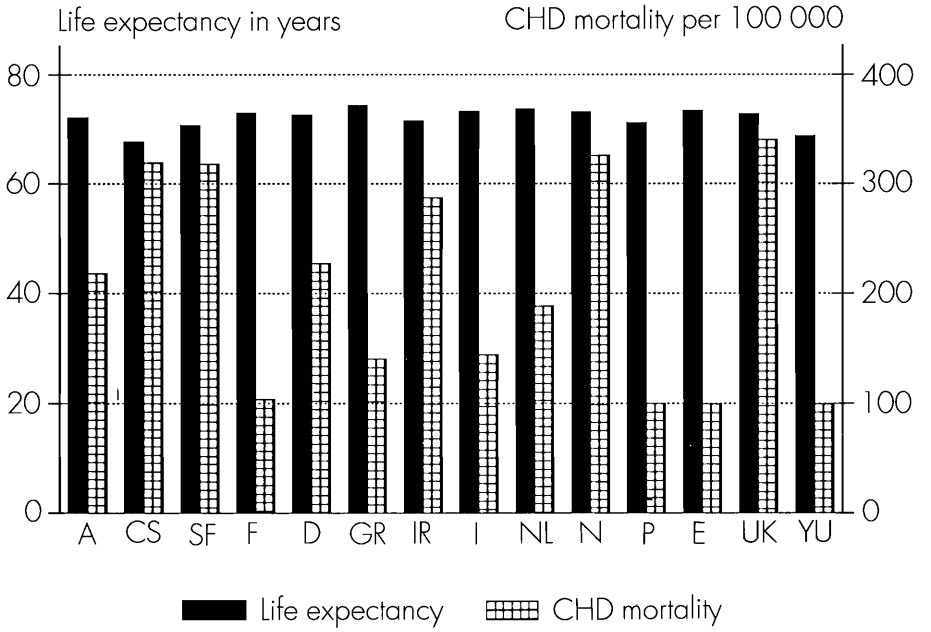
Fig. 3, in which coronary heart disease mortality and life expectancy for males is displayed simultaneously, clearly shows that there is no relationsship between the coronary heart disease death rates and life expectancy in these fourteen countries.

The main source of diagnostic information concerning cause of death is the *death certificate*. What one reasonably may conclude from these three figures is that for some reason or another, doctors in the Mediterranean countries do not put «coronary heart disease» as a cause of death on the death certificate. In other words, the statistics concerning coronary heart disease prevalence are based on



Source: World Health Statistics Annual 1990

Fig. 2: Life expectancy in 14 European countries



Source: World Health Statistics Annual 1990

Fig. 3: Life expectancy and CHD mortality in males

apparently misleading information. We will not conjecture as to which end of the spectrum of high or low coronary heart disease prevalence is correct - there is simply not sufficient information to make an informed guess. There is no inherent strength in diagnostic mortality information - it is used mainly because that is only thing we have.

Even if the registration of coronary heart disease mortality (let alone morbidity) were uniform from country to country, it would not necessarily mean that morbidity prevalence was uniform. This is due to the fact that a diagnosis is not the same as a clear definition of a disease pattern. Coronary heart disease as a diagnosis is perhaps not the worst catch-all in this regard, but it certainly lacks precision as a definition of patient condition. Even in the case of a relatively well-defined and narrow disease pattern, e.g. insulin dependent diabetes mellitus, variation in the natural course of the disease in the individual patient and many factors having to do with patient compliance with disease management will determine the placement of the individual along a spectrum of mortality outcomes. Returning to coronary heart disease, the point is that it doesn't improve your overall life expectancy to eat the (perhaps) more palatable Italian diet than the less palatable English diet, merely something else appears on your death certificate. Overall mortality is generally recorded fairly accurately in all countries, so that is at least what one can call «hard data».

Meanwhile, a proverb from the folklore of Persia illustrates a problem with these data, i.e. that death does not wait while one decides what to die of: *An old master is surprised by his young gardener, who comes to ask him for his fastest horse, as he has to be away tonight. The old master asked him why he was so excited, has something happened? The gardener told him he saw Death while he was working in the garden, and Death threatened him. He realized he had to hide on a farm, otherwise Death would get him. So the master gave him the horse and the gardener rode away to the farm. Later, the master was walking through the garden, and he also saw Death. He asked Death, why do you threaten my gardener? And Death answered; I was not threatening him, I just wondered what he was doing here, as I was supposed to meet him tonight on the farm.*

Taking a more global view of the problem, *Fig. 4* depicts patterns of mortality of coronary heart disease from 26 countries. The data stem from six observation periods over a total of thirty years, between 1950 and 1980. At the top are trends for men, with trends for women at the bottom. One will notice something peculiar: with the exception of *Finland*, the highest mortality rates are from the English-speaking countries. One might conclude on the basis of these data that *English as a mother tongue* is the strongest risk factor for dying of coronary heart disease. Another conclusion might be that English language doctors are more

heavily motivated, for whatever reason, to put «coronary heart disease» on the death certificate than their non-English language counterparts. (The exception of Finland may have to do the lifestyle of the Finns - they go to the sauna and then run out and roll in the snow and die of a heart attack. It may also have to do with an even higher motivation on the part of the Finnish doctors to put coronary heart disease on the death certificate.)

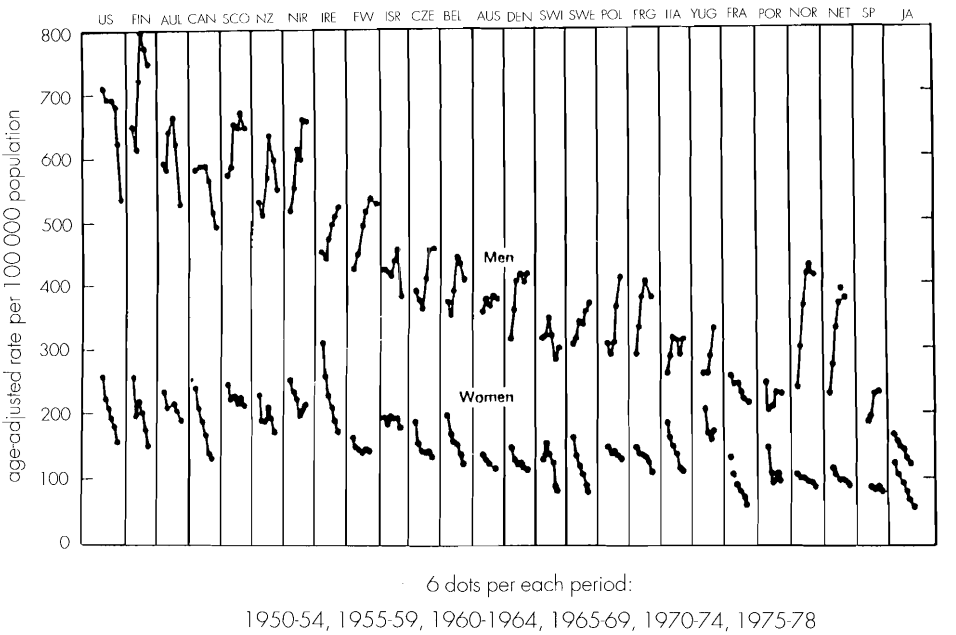


Fig. 4: Trends in mortality from heart disease in men and women of age 45 to 64 in twenty-six countries, 1950 to 1978

Returning to *Fig. 4*, the experts who say that diet is a major factor disposing to coronary heart disease have yet another problem to explain. One can see that in Ireland or Sweden, for example, the trend for female mortality by coronary heart disease is downwards over time while the trend for male mortality is upwards. Unless one is prepared to believe that males and females eat significantly differently, that difference is not explainable by cholesterol consumption. The experts counter that cholesterol is only one of many risk factors which interact in a multifactorial fashion. They maintain that one must not be oversimplistic, for we know that there are more than 350 risk factors recorded for coronary heart disease.

The risk factors for coronary heart disease include old faithfuls, such as smoking, overeating, family history and high blood pressure, and a plethora of more or less believable others, including not exercising, not having siestas, not eating

fish, speaking English, type A personality (whatever that is), snoring, an earlobe crease, being male, and perhaps most optimistically, being poor (because that can be altered). What does this mean, what is a risk factor?

In the epidemiological use, a risk factor has predictive power in the predilection towards morbidity. It does not confer causality by definition, although some causality may be there. It does not mean, for example, if an earlobe crease is associated with coronary heart disease, that cutting off the creased ear will diminish the risk. The experts have for some reason focused on blood cholesterol, and some have found it (mistakenly, as will be demonstrated below) to be positively correlated to coronary heart disease mortality. They are saying that if one reduces cholesterol consumption, then coronary heart disease incidence will diminish.

Another way to interpret this multifactorial «theology» is that the experts are really saying that they have no clue. They are in the same position as the doctors were 200 years ago when they didn't know the cause of scurvy. They used the same sort of reasoning, namely: Could we associate the prevalence of the disease with certain risk factors? They discovered lots of risk factors, which are strikingly similar to those of modern diseases. The first one is bad diet. They always go for bad diet if they don't understand the cause of the disease. Then having sex, of course, could have something to do with it, and people who smoke and drink are always dangerous. This was a disease of sailors. An obvious risk factor was sea air. There was a very strong relationship: the more you are exposed to the sea air, the more likely you were to get the disease. This is the sort of reasoning we use now in the area of diet, cholesterol and coronary heart disease. (Ask the experts, and they will provide an *ad hoc*, on the spot consensus!)

This is a typical example of the **ecological fallacy**, of which there are numerous examples in the literature. One of the more recent and blatant examples came from the Framingham study (see also below), in which coffee drinking was suddenly implicated as a risk factor for coronary heart disease. The report was refuted a mere few weeks after its publication. It turned out that coffee drinking habits are associated with other risk factors, especially smoking, and coffee drinking had no predictive power on its own. This type of error often occurs in connection with multivariate analyses, since the models used tend to be more sophisticated than the scientific questions they are designed to answer. Indeed, as in the coffee scare, the model raises the question ad hoc out of data which were gathered for other purposes. This problem is exasperated by a prevalent tendency to prioritize statistical excellence in front of research methodological excellence, a tendency which unfortunately is encouraged by some journal editors in their article selection process.

There is much public commotion about cholesterol. In the United States there

is a tradition of declaring war on things. There has been a war on drugs for a long time, and a war on crime, and now there is a war on cholesterol. There is a well-known poster published by the *American Medical Association (AMA)* which represents the enemy creeping up in the middle of the night - if you swallow these tablets, nothing will happen to you (if you eat garlic the vampires will not get you). There are any number of scams of this nature in society. KARL MARX said, «The people will have their opium.»

The question is: does this have a place in the medical world? There is a lot of money in the war on cholesterol, of course. Cholesterol screening sets are advertised in papers with a promise of up to US$ 50,000 per annum income for an entrepreneurial couple - ideal for a husband-wife operation!

The cholesterol fallacy

Apart from all of this public commotion, what is the evidence that cholesterol in the diet has anything to do with coronary heart disease? The evidence comes in four levels of relevance *(Tab. 1)*.

A. Animal experimentation	
B. Epidemiology	(1) CHD trends - dietary correlations (2) CHD rate - inter-country correlations (3) CHD rates - migration studies
C. Human observational studies	(1) Biochemical: Diet effect on blood lipids (2) Pathology: Lipids - atherosclerosis Atherosclerosis - CHD (3) Clinical: Blood lipids - CHD Diet - CHD
D. Intervention studies	(1) Single risk factors: - diet trials - cholesterol-lowering drugs (2) Multiple risk factors

Tab. 1: Levels of evidence for diet-heart hypothesis

The *poorest evidence* comes from animal studies, where rabbits fed with enormous amounts of cholesterol developed very peculiar degenerative conditions. Rabbits do not usually eat cholesterol-containing foods, and feeding them with such (animal fat) makes them very sick. Surely, one cannot make any comparison from these observations to humans.

Of this same degree of *spurious evidence* is the so-called *Seven Countries Study*. In the seven countries investigated, fat consumption and death rates from coronary heart disease were plotted on an X-Y graph. A line was drawn through the

points (linear correlation), and the authors concluded that the higher the rate of fat consumption, the more deaths from coronary heart disease. Unfortunately for this conclusion, if one uses the data for protein consumption instead, an even better correlation appears. Why not draw correlations between coronary heart disease death rates and those who wear hats, of suspenders, of those who sleep on their right side? The only conclusion one can draw from this kind of study is that it is possible to pick suitable data for any preconceived hypothesis.

The *next level of evidence* is somewhat better. It comes from *cohort studies*, the most famous of which in the coronary heart disease field is the *Framingham study* from Massachusetts, USA (also mentioned above).

The design of the study was to measure health status for a population, follow the population while monitoring a range of known and unknown disposing factors to coronary heart disease, and record who in the population develops coronary heart disease and who does not. It was thought that this would shed light on the relative weights of various risk factors for coronary heart disease. Blood cholesterol levels were one of many different factors studied, and these values were plotted for those who developed coronary heart disease and those who did not. The resulting plots *(Fig. 5)* overlap to the extent that for practical purposes there is no real difference between the two groups. In other words, it is not possible on the basis of the cholesterol level to predict who will develop coronary heart disease and who not.

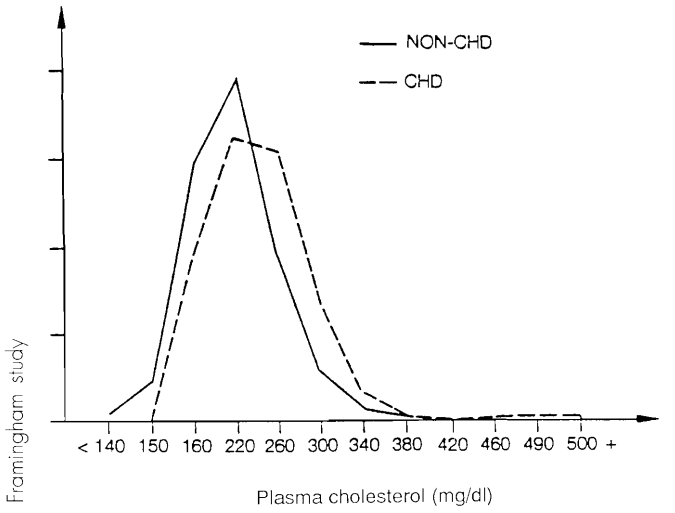


Fig. 5: Plasma cholesterol in men initially aged 30 to 49 years who stay free of coronary heart disease (NON-CHD) or develop coronary heart disease (CHD) during 16 years follow-up

An analysis of the same study, published in a supplement which is very difficult to obtain as it is missing in libraries *[Int J Epidemiol 1989; 18 (suppl. 1): S67-72]*, showed a very peculiar result: In 1953, 38% of the middle-aged men in *Framingham* had a high cholesterol of ≥240 mg% and 56% were smokers. 20 years later, after all this anti-cholesterol, anti-smoking, blood pressure, exercise and life style intervention, smoking and cholesterol consumption in fact went down. In the same time, however, the prevalence of coronary heart disease in men **increased** by over 50% (102 per 1000 in 1953, 134 in 1963, and 159 in 1973) and coronary heart disease mortality remained the same (93 per 10,000 in 1953, 84 in 1963, and 99 in 1973). In other words: according to the *Framingham* data there are more people walking around with the diagnosis of heart disease than ever before and the rate of death is exactly the same as it always was.

In spite of this contrary evidence the *Framingham study* is the most widely cited source of confirmation that the calorie-rich, high-cholesterol and high-saturated fat diet contributes to the development of coronary heart disease, and furthermore, that blood cholesterol is the main enemy.

A second large cohort study is from Finland, the *North Karelia study*. As mentioned above, the data suggest that Finland has the highest rate of coronary heart disease in the world, and in Finland, the highest rate of coronary heart disease is in the county of North Karelia (not to forget the problems with death certificates and diagnoses as described above). So it was decided to run a community intervention. The study designers used the risk factor theory, namely, to reduce the cholesterol content in the diet, control blood pressure, and reduce smoking, in order to reduce the incidence of coronary heart disease. The project started in 1972, and the initial analysis was done after five years.

As shown in *Fig. 6*, coronary heart disease in *North Karelia* was reduced beautifully, and the advocates thought that that proved it, it clinched the argument.

In fact, the advocates would be likely to make this claim no matter what the study showed. Meanwhile, when similar data were compiled for the other Finnish counties, in which no intervention was implemented during the same time period, exactly the same development appeared - the same reduction and even the same rate of reduction. In other words, the data suggest that the reduction was the result of factors with which the intervention had nothing to do. Yet, this study is often used by the advocates as proving their diet-lipid hypothesis. Not evaluated in the study was the issue of whether something had changed in the registration of coronary heart disease mortality.

The *best level of knowledge* («the proof of the pudding») comes from randomised controlled trials: are divides people into two groups, manipulate the risk factors

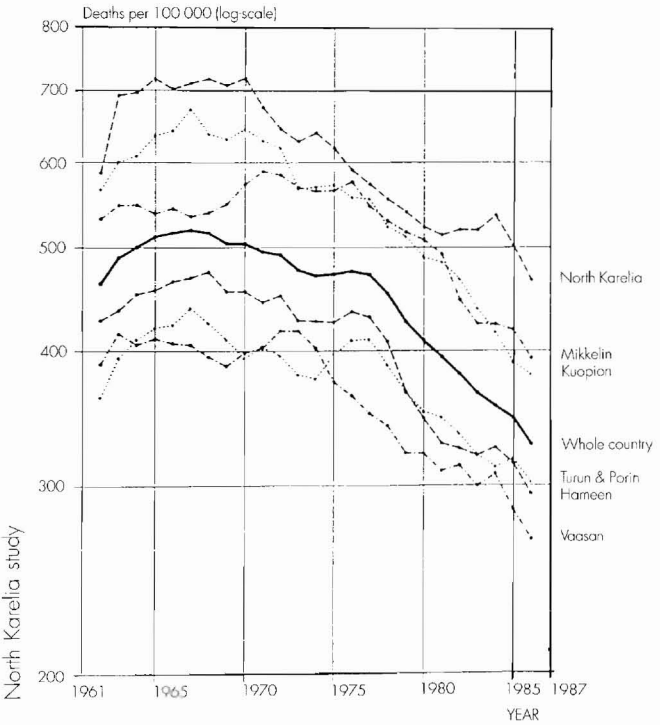


Fig. 6: Trends in age-standardised CHD mortality in several Finnish counties, 1961-1987

in one, leave the other alone, and after a certain period see whether there is a difference in the outcome of heart disease and the overall mortality.

In the *Lipid Research Clinics Trial*, 3806 men with high blood cholesterol levels were followed for seven years. The men were divided into a treatment group, who had their blood cholesterol levels lowered by the drug *cholestyramine*, and a control group, who received a placebo. At the end of the observation period, there was no significant reduction in coronary heart disease related mortality in the treatment group. The observed difference of 20% was underlined in the report and subsequently gobbled up by the anti-cholesterol mafia, but not underlined was a similar increase in mortality from other causes in the treatment group! In other words, this study shows, if anything at all, that the treatment for high blood cholesterol is about as dangerous as having high blood cholesterol (see also contibution by GEORGE DAVEY SMITH on page 42 in this book). The actual numbers from the trial are presented in *Tab. 2*

End point	Cholestyramine (n=1906)	Placebo (n=1900)	% reduction in risk	Risk difference per 1000 yrs.	p-value
Myocardial infarction (fatal and non-fatal)	155	187	17	2.4	0.065
CHD death - definite	30	38	21	0.6	0.32
- suspected	32	44	27	0.9	0.16
Death from other than suspected CHD	36	27	- 33	- 0.7	0.26
All-cause mortality	68	71	4.5	0.2	0.78

Tab. 2: Definite primary end-points and all-cause mortality in the Lipid Research Clinics Coronary Primary Prevention Trial

There are two important things to remember when assessing these figures, or any other figures from studies of this nature. The first is the issue of statistical significance, and the second and more important issue is whether the difference, when and if established, means anything.

In this case there is no formal statistical evidence that there is any difference in the number of myocardial infarctions or coronary deaths occurring in the treatment contra the non-treatment group. More importantly, the mortality differences have no practical significance. The difference is 8 coronary deaths among 4,000 people in 7 years (or a difference of just 0.5 per 1000 person-years). As per the age-old proverb above, the study shows expectedly that people live and people die, and blood cholesterol levels do not influence these two facts to a significant degree.

On the practical side of this academic exercise, it turns out that for each of the 8 lives presumed saved in this way, on the order of 10 metric tons of *cholestyramine* with a market value of somewhere on the order of 2 million US$ had to be consumed. It is not difficult to imagine what drives the producers of blood cholesterol-lowering drugs to fuel the cholesterol scare. In comparison, one might think for a moment of a drug which really has some impact, say, penicillin. No one would dream of doing a randomized controlled trial of mortality from pneumonia with or without penicillin. Doing the experiment as a thought exercise, however, will tell us that the number of lives saved is enormous, the amount of the drug consumed per life saved is on the order of only several grams and has a market value of only several US$. The point is that there is a level of insignificance about the whole cholesterol issue which beggars the concept.

What about other trials? There have been only five multifactorial intervention trials *(Tab. 3)* which assess the established risk factors, smoking, high blood pressure and sedentary life style, together with blood cholesterol [see *Lancet 1988; II: 839-841* and the newest Helsinki study figures in *JAMA 1991; 226: 1225-1229*]

Trial	CHD deaths I	CHD deaths C	Total deaths I	Total deaths C	Lives saved per 1000/yr
WHO	428	450[1]	1325	1341[1]	0.1
Göteborg	462	461	1293	1318	0.2
MRFIT	115	124	265	260	excess deaths
Helsinki	34	14	67	46	excess deaths
Oslo	6	13[1]	16	23[1]	2.3

(1)Adjusted for the difference in sample size in the intervention (I) and the control (C) groups.

Tab. 3: Mortality outcome of the five multiple risk factor intervention trials

As one can see from *Tab. 3*, with the possible exception of the Oslo trial, the number of lives saved were far from impressive. The Oslo trial is an exception, and one can look at this difference from a variety of angles. Some would be tempted to exclaim, «Look, we finally proved it!», but we would rather believe that we here have an example of the type I statistical error, i.e. showing something which is a chance result and does not really exist. The deaths are real, but is it reasonable to believe that this one study refutes all the other negative ones when the basic premises were the same? The results certainly need to be reproduced in a larger population before we can accept the intervention described in the Oslo trial as effective.

Taking the figures in one overall view, there is a difference of 13 excess deaths in the control groups over a total of close to 900,000 man-years observed. In comparison, one may ask if anyone would wonder at 13 more deaths in town A than in town B, both with populations of approx. 450,000 and an expected number of deaths in a given year of approx. 4500?

An interesting twist on these trials is the multiple risk factor intervention trial with Finnish executives (the *Helsinki study* in *Tab. 3*) - the investigators succeeded in indoctrinating these anxious executives to do everything «right»: To exercise more, eat the right thing, not to smoke and so on. They managed to reduce their risk factor index by 50%. Meanwhile, the men with reduced risk factor

indices were the treated patients, so the incidence of coronary heart disease actually increased 150%. In other words, the reduction of the risk index increased the incidence of the disease.

Summarizing all of this, it is likely that there has been no other treatment in medical history which has so conclusively been proven to be ineffective. Yet, it continues to be one of the major unshakeable dogmas in current medical teaching that cholesterol and heart disease are linked. In other words, the issue is a fad, and there is no conceivable experiment which would change the minds of the believers or, if you wish, the apostles of this cholesterol hypothesis.

The last thing to consider is the rationalisation that it cannot do any harm to reduce the risk factors. «It cannot do any harm, it will not hurt» is akin to having a salesman, who is selling a *hoover,* make a mess on your carpet, throw cigarette butts, fluff and dirt on it and then switch wich on the *hoover*, does not pick the dirt up. You would say: «That's no good!» And the salesman says: «But it didn't blow the fuse, did it? It didn't do any harm.» Can you sell anything with this sort of argument?

Who profits from this? The list is long: drug companies, obviously, certain parts of the food industry (notices appearing on foodstuffs saying «Cholesterol Free»), doctors gaining income from prescriptions and follow-up visits, and last but not least, the screening industry.

The big losers in this game are the public, who through the media and via their doctors are bombarded with advertisements citing 20, 30, even 67% reductions in development of coronary heart disease through blood cholesterol-lowering medication. Meanwhile, somewhere in the small print one will find that in some studies, more patients died in the treatment group than in the control group, and in other studies, significant increases in liver carcinomas were observed in rats eating large quantities of the drugs. Nowhere in the small print is it expressed that the evidence massively refutes the idea that blood cholesterol reduction lowers the burden of disease. In other words, we are guilty of prescribing drugs with no proven benefit and with well established detriments, the most scary of which is payment for a drug which has no effect and may kill some people. Furthermore, science suffers, because knowledge is being trod under foot by salesmen who are insensitive to issues other than the monetary.

It would be well if this were an isolated event. Unfortunately, this is only the tip of the iceberg, and medical reasoning suffers. We have let ourselves be duped by a bandwagon where the blind lead the blind. We hope to have provided some tools to those who would help stop the unethical practice of wasting resources on useless treatments, and we further hope to have demonstrated a problem-

solving mode, a conceptual framework if one will, for pulling the carpet out from under the feet of those who would corrupt science for the sake of personal gain. The idea of promoting cholesterol as an evil to whole nations and putting everyone on a «correct» diet, and a large proportion on life-long medication, is scientifically unjustified, medically foolish and politically ominous.

Further reading

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