FACT SHEET 1

$TATIN NATION

The Great Cholesterol Cover-Up

Documentary film: 63 minutes

www.statinnation.net

Background

The basic idea is that dietary saturated fat raises cholesterol levels, and these two substances somehow clog-up our arteries causing a heart attack. The *diet-heart hypothesis* also known as the *cholesterol hypothesis*, has for many years been the focus of heart attack prevention strategies around the world.

It is important to note the word "hypothesis" above. The fact is that these ideas have never actually been proven. The origins of the hypothesis can be traced back to a researcher who worked at the University of Minnesota by the name of Ancel Keys.

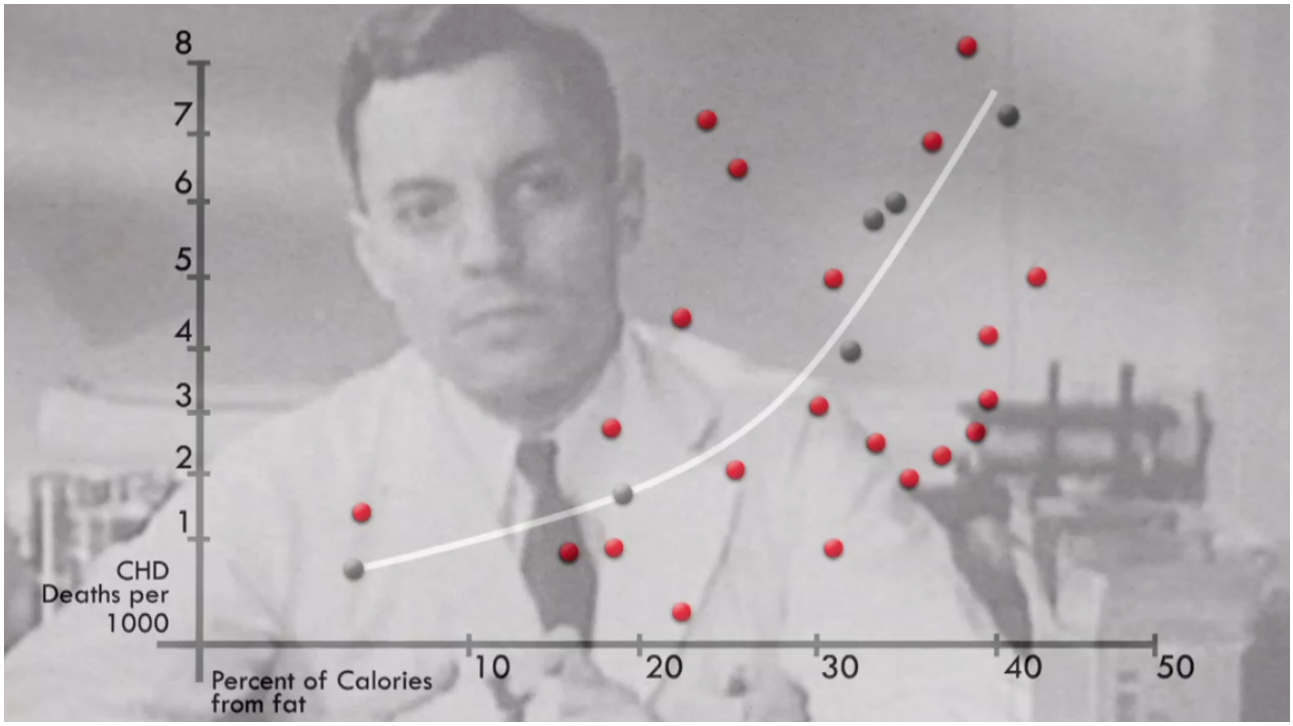


Figure 1. Graphic showing the six datapoints chosen by Keys in grey and the data Keys omitted as red points.

Ancel Keys published his now infamous six countries study in 1953, where he plotted on a graph the dietary fat intake of six countries against the numbers of deaths from heart disease (1). His graph showed a straight line relationship between higher fat intake and increased mortality. However, at the time of the study, there were data also available for another 16 countries. Keys omitted these 16 countries from his study because they did not fit his suggested linear relationship (2).

Keys, of course, was not solely responsible for the adoption of the diet-heart hypothesis, but at the time he was a well-known researcher and his influence was pivotal. Hence, he is widely regarded as the 'father' of the hypothesis.

Contradictions to the Cholesterol Hypothesis

If the diet-heart hypothesis was valid, we would of course expect to find that countries having a high rate of heart attacks, also have higher cholesterol levels. This is not the case. For example, the United Kingdom had one of the highest rates of coronary events (a severe heart problem such as a heart attack) at the same time as having a below average cholesterol level for Europe (3,4,5).

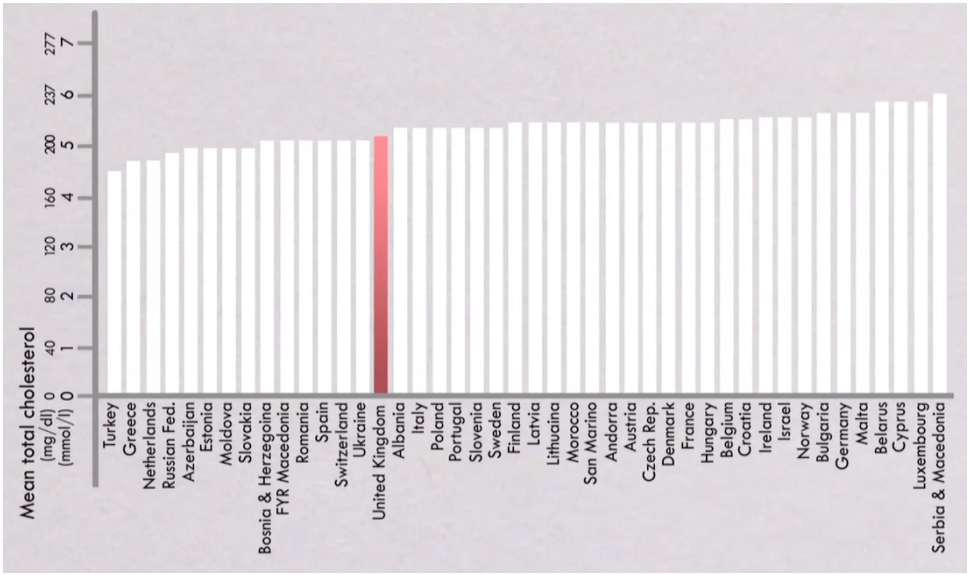


Figure 2. Average cholesterol levels for men in the UK are the 15th lowest on a scale of 45 European countries. Data published by the British Heart Foundation.

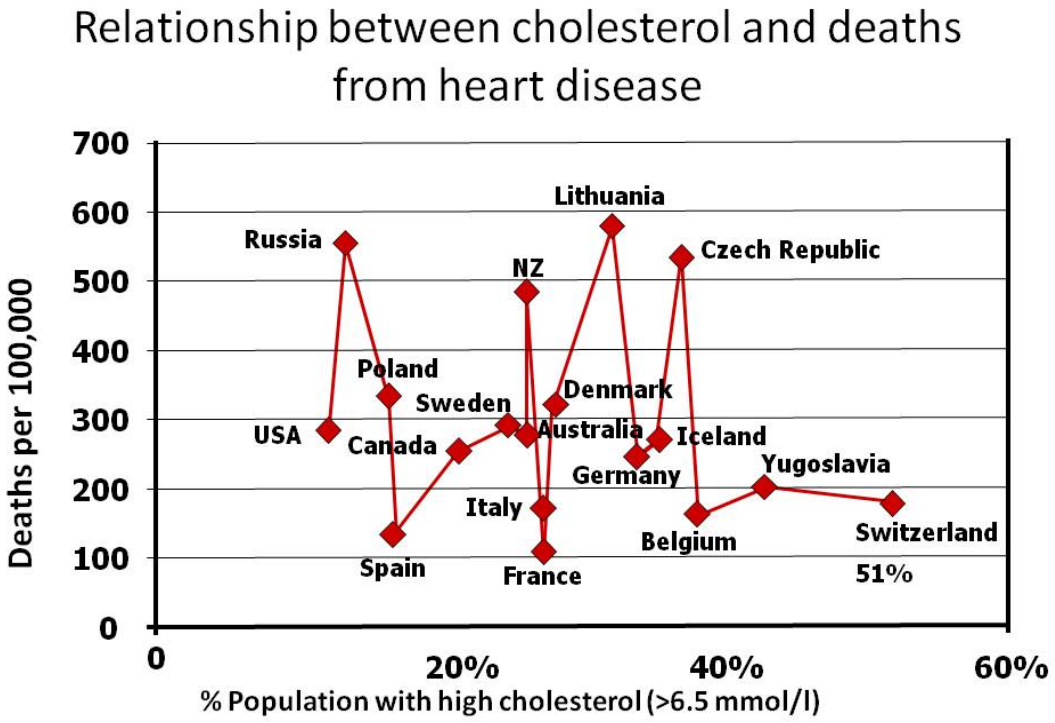
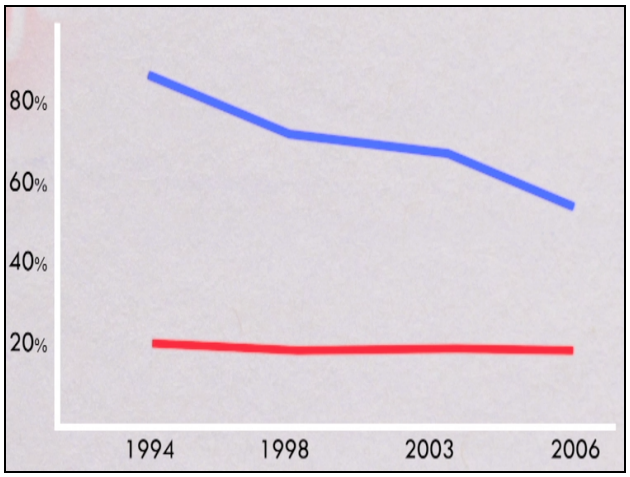


Figure 3. Comparing the percentage of people with high cholesterol with the rate of deaths from heart disease. Graph courtesy of Barry Groves PhD, author of Tick and Treat: How healthy Eating is Making Us Ill. Data from World Health Organisation MONICA study 2005.

The example of the United Kingdom has been chosen to illustrate the point. But this is by no means an isolated case. When we look at the data, there is no correlation whatsoever between the cholesterol levels of a particular country and that country's rate of heart attacks/coronary events, or even the rate of deaths from heart disease – as illustrated in figure 3.

In addition, cholesterol-lowering on a population level does not reduce the rate of heart disease. For example, there have been large reductions in the number of people with "high cholesterol" in the UK, but the rate of heart disease has stayed the same (figure 4).



Year	Percentage of Men (65 to 74 yrs) with High Cholesterol	Prevalence of CHD
1994	87%	21%
1998	76%	20%
2003	69%	22%
2006	54%	21%

Figure 4. The proportion of men between the ages of 65 and 74 in the UK with "high cholesterol" has reduced almost 40%, but the rate of coronary heart disease (CHD) has stayed the same. Data published by the British Heart Foundation (6,7).

Another way to investigate the causes of heart disease might be to look at the differences between different socioeconomic groups.

People with a low income have a much higher risk of dying of heart disease. For example, in England, men in the lowest socioeconomic group are almost 3 times more likely to die of heart disease than men in the highest socioeconomic group.

We might expect, therefore, that there are more people with high cholesterol in the lowest socioeconomic group. However, the reverse is true; the lowest socioeconomic group have fewer people with high cholesterol.

Women in England, in the lowest socioeconomic group are 5 times more likely to die of heart disease than women in the highest socioeconomic group, but have approximately the same number of people with high cholesterol (figure 5).

All of the experts agree that heart disease is a complex condition, with several contributing factors, however, this data raises questions about the the importance of high cholesterol.

Figure 5. Women in England, in the lowest socioeconomic group are 5 times more likely to die of heart disease than women in the highest socioeconomic group, but have approximately the same number of people with high cholesterol (8, 9).

"Bad" Cholesterol

When we have a cholesterol test, the results are usually described in terms of "good" cholesterol and "bad" cholesterol. The "good" cholesterol is called HDL and the "bad" cholesterol is called LDL.

Cholesterol-lowering medications, in particular, statins, are prescribed to lower "bad" cholesterol levels (LDLs). However, a large study published in the *American Heart Journal* in 2009 found that the level of so called "bad" cholesterol is actually lower in people with heart disease, not higher.

This study included around 137,000 people who had been admitted to hospital with heart disease. It included patients from 541 hospitals in the United States. All of these people had their LDL level measured within 24 hours of admission (10).

The researchers found that the average LDL level for this group of people was actually lower than the average level for the American general population (10, 11, 12).

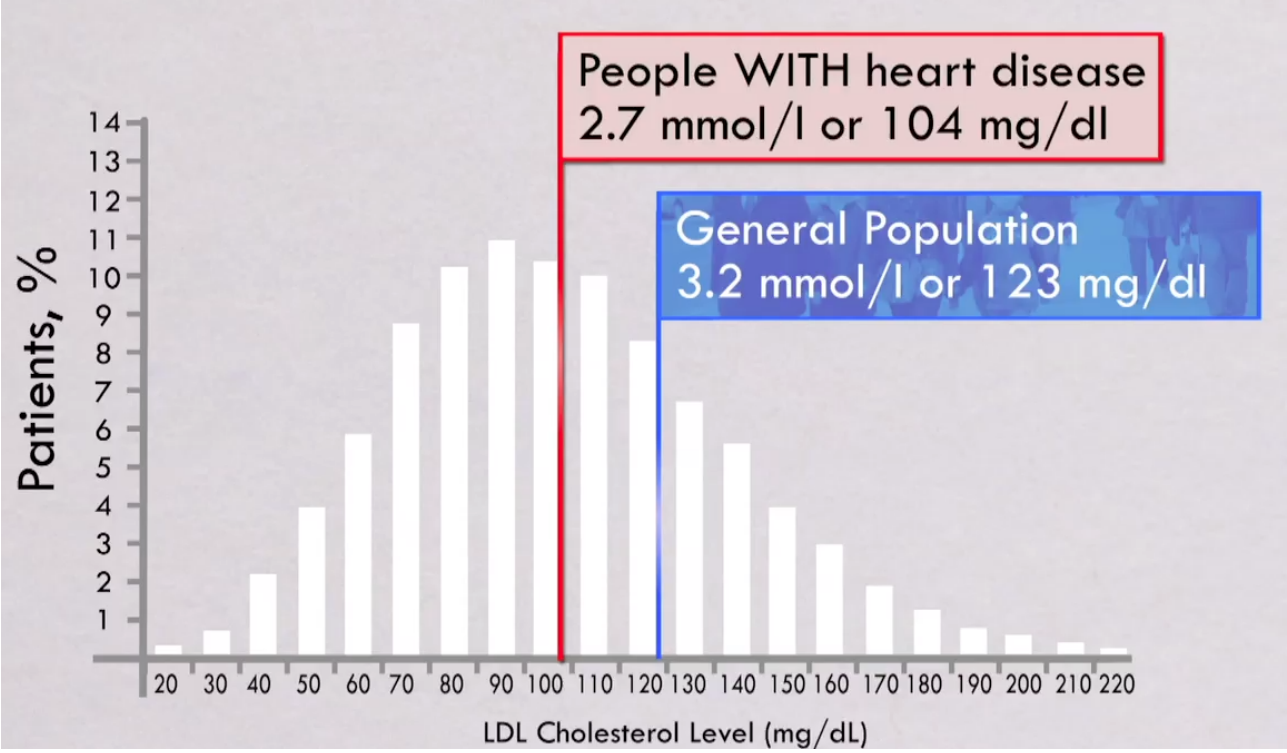


Figure 5. People admitted to hospital in the United States with coronary artery disease had lower levels of so called "bad" cholesterol than people in the general population.

The average level for people with heart disease was 104 and the average for the general population was 123. This data raises the obvious question - if people with heart disease have lower levels of so called "bad" cholesterol, why are some countries around the world spending billions of dollars each year lowering these levels?

Cholesterol-Lowering Medications (STATINS)

Around 75% of all the people who take a statin, are taking it for *primary prevention*. This means they do not have a heart problem but are taking the medication in the hope of preventing a heart problem in the future. When it comes to primary prevention none of the largest clinical trials have been able to conclusively show any net benefit.

The AFCAPS (13), ASCOT (14), CARDS (15), PROSPER (16) and WOSCOPS (17) clinical trials all failed to show a statistically significant reduction in all cause mortality (deaths from all causes, not just heart disease related deaths).

All cause mortality data, of course, is the only true measure one can use to determine if a statin is going to extend life expectancy or not. Whilst some clinical trials of statins have shown a very slight reduction in heart disease, in primary prevention, this has always been countered by deaths from other causes. The net result is that people do not live any longer after taking a statin.

In 2008, pharmaceutical companies and much of the world's media trumpeted the results of the JUPITER trial. If we take a closer look at the data from this trial, it can be seen that serious cardiac events (termed “hard cardiac events”) were reduced by less than one percent (18).

The situation could be even worse than that, since an article published in the *Archives of Internal Medicine* in 2010 questioned the validity of the data from the JUPITER trial and raised concerns about the role of the company sponsoring the trial (19). Another article published in the journal *Cardiology* in 2011 raised similar concerns (20). These critical papers were not given the same prominence within the medical journals as was given to the JUPITER trial results and were not mentioned in the mainstream media at all.

In 2010, a meta-analysis of 11statin trials was published in the *Archives of Internal Medicine*. Professor Kausik Ray and colleagues concluded that statins provided no benefit in terms of deaths from all causes, when used for primary prevention (21). This analysis had the “cleanest” dataset of any analysis completed to date - the researchers were able to exclude patients with existing heart disease (known as secondary prevention) and only include data associated with primary prevention.

In 2011, the highly respected *Cochrane Collaborative* conducted a review of statin clinical trials. Based on this, lead authors Dr Shah Ebrahim and Dr Fiona Taylor said that they could not recommend the use of statins for primary prevention. The absolute benefit was so small that it could have been down to chance, and even if it was a real benefit, 1000 people would have to be treated for one year to prevent one death (22).

When we look at the use of statins for people who already have a diagnosed heart problem (the 25% of people, in secondary prevention) the picture becomes less clear cut. Some trials have found significant increases in life expectancy for these people, however, the trials have always been too short for us to assess the long-term impact of being on a statin.

Even if statins do provide a short-term benefit for those with a heart problem, it is debatable that this has anything to do with the cholesterol-lowering effect of statins. Quite simply, the amount of benefit does not match up with the degree of cholesterol-lowering. The potential beneficial affects of statins for people with heart disease is now widely recognised to be associated with a reduction in inflammation. And recent evidence suggests that this is mediated through an improvement in iron metabolism (23).

References and Footnotes

1. Keys, A. Atherosclerosis: a problem in newer public health. Journal of the Mount Sinai Hospital, New York. 1953 Jul-Aug;20(2):118–139.
2. Ravnskov, U. The Cholesterol Myths: Exposing the Fallacy that Saturated Fat and Cholesterol Cause Heart Disease. Newtrends Publishing, 2000.
3. Allender S, Peto V, Scarborough P, Kaur A & Rayner M. 2008 Coronary Heart Disease Statistics. Chapter 10 Blood Cholesterol (Figure 10.7a on page 183) British Heart Foundation, London.
4. Allender S, Scarborough P, Peto V, & Rayner M. 2008. European Cardiovascular Disease Statistics. Chapter 2 Morbidity (Table 2.1 on page 38). British Heart Foundation, London
5. Given the importance that is placed on cholesterol and the resources allocated towards cholesterol-lowering, it is surprisingly difficult to find actual data that compares cholesterol levels against the rate of heart attacks/coronary events for different countries/populations. The quest becomes even more challenging when finding comparative data for the same time period. One of the very few sources available is the *World Health Organisation's MONICA project*. This data has been used by the British Heart Foundation in their publications on cardiovascular disease statistics. For comparison, two publications have to be consulted: European Cardiovascular Disease Statistics 2008, and Coronary Heart Disease Statistics 2008. In order to compare the rate of heart attacks/coronary events against cholesterol levels for various countries, around the same time period, you have to cross reference data from these two separate reports. Another article published in the *Lancet* around the same time, also showed that the UK populations studied had one of the highest rates of heart attacks/coronary events (*Lancet 1999;353:1547 - 1557*) It is also worth mentioning that the British Heart Foundation have published a very detailed and well presented report in 2011 titled 'Trends in Coronary Heart Disease, 1961-2011'. However, interestingly, no data on cholesterol levels is included in this report.
6. Allender S, Peto V, Scarborough P, Kaur A & Rayner M. Coronary Heart Disease Statistics 2008. Chapter 10 Blood Cholesterol (Table 10.2). British Heart Foundation, London.
7. Allender S, Peto V, Scarborough P, Kaur A & Rayner M. Coronary Heart Disease Statistics 2008. Chapter 2 Morbidity (Table 2.10). British Heart Foundation, London.
8. Scarborough, P et al. Coronary Heart Disease Statistics 2010. British Heart Foundation Health Promotion Research Group, Department of Public Health, University of Oxford.
9. Scarborough, P et al. Regional and Social Differences in Coronary Heart Disease 2008. British Heart Foundation Health Promotion Research Group, Department of Public Health, University of Oxford.
10. Sachdeva A et al. Lipid levels in patients hospitalized with coronary artery disease: an analysis of 136,905 hospitalizations in get with the guidelines. American Heart Journal 2009; 157: 111–117.
11. Carroll MD et al. Trends in serum lipids and lipoproteins of adults, 1960–2002. Journal of the American Medical Association 2005; 294:1773–1781.
12. For comparison, the LDL level of people 20 years and older was used. However, women around the same age as those included in the American Heart Journal study (10) had an LDL level of 133 and men around the same age had an LDL level of 127 mg/dl – which means that in real terms, the difference was even more significant. According to the American Heart Association the average level of LDL cholesterol for American adults age 20 and older is 115 mg/dL (http://www.heart.org/HEARTORG/Conditions/Cholesterol/AboutCholesterol/What-Your-Cholesterol-Levels-Mean_UCM_305562_Article.jsp accessed March 14, 2013).

13. Downs JR, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. JAMA 1998; 279:1615-22.
14. Sever PS, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. Lancet 2003; 361:1149-1158.
15. Clhoun HM, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atovastatin Diabetes Study (CARDS). Lancet 2004; 364:685-696.
16. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet 2002; 360:1623-1630.
17. Shepherd J, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia (WOSCOPS). N Engl J Med 1995; 333:1301-1307.
18. Ridker, PM et al, for the JUPITER Study Group. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. N Engl J Med 2008; 359:2195-207.
19. de Lorgeril, M et al. Cholesterol lowering, cardiovascular diseases, and the rosuvastatin-JUPITER controversy. A critical reappraisal. Arch Intern Med. 2010; 170:1032-1036.
20. Serebruany, VL. Extreme all-cause mortality in JUPITER requires reexamination of vital records. Cardiology. 2011; 120:84-8
21. Ray KK, et al. Statins and all-cause mortality in high-risk primary prevention: a meta-analysis of 11 randomized controlled trials involving 65,229 participants. Arch Intern Med. 2010; 170:1024-31.
22. Hughes, S. Cochrane review stirs controversy over statins in primary prevention. TheHeart.org. January 20, 2011
23. Zacharski, LR et al. The Statin–Iron Nexus: Anti-Inflammatory Intervention for Arterial Disease Prevention. American Journal of Public Health. Published online ahead of print February 14, 2013.