Cholesterol: Wrong Target for Primary Prevention of Cardiovascular Disease?
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We have all been led to believe that cholesterol is bad and that lowering it is good. Extensive pharmaceutical marketing of statins to both doctors and patients lead us to believe that their benefit is proven to lower the risk of heart attacks and death.

But on what scientific evidence is this based, was does that evidence really show?

Roger Williams once said something that is very applicable to how we commonly view the benefits of statins. “There are liars, damn liars and statisticians.

We see prominent advertisements on television and in medical journals that statins therapy results in a 36% reduction in the risk for a heart attack. What does that REALLY mean and what does it affect decisions about who should really be using these medication?

Consider the following:

- If you lower LDL-C but have a low HDL there is no benefit to statins.\(^i\)
- If you lower LDL-C but don’t reduce inflammation (C-reactive protein), there is no benefit to statins.\(^ii\)
- If you are a healthy woman with high cholesterol, there is no proof that taking statins reduces your risk of heart attack or death.\(^iii\)
- If you are a man or a woman over 69 years old with high cholesterol, there is no proof that taking statins reduces your risk of heart attack or death.\(^iv\)
- ENHANCE: Aggressive cholesterol treatment with two medications (Zocor and Zetia) lowered cholesterol much more than one drug alone, but led to more plaque build up in the arteries and no fewer cardiac events.\(^v\)
- 50-75% of people who have heart attacks have normal cholesterol.\(^vi\)
- Older patients with lower cholesterol have higher risks of death than those with higher cholesterol.\(^vii\)
- Countries with higher average cholesterol than Americans such as the Swiss or Spanish have less heart disease.
- JUPITER: Recent evidence shows that it is likely statins ability to lower inflammation that accounts for the benefits of statins, not their ability to lower cholesterol.\(^viii\)

So whom do the statin drugs work for anyway? They work for secondary prevention in those who have had cardiac events to prevent further cardiac events or death. The evidence is clear for secondary prevention. And they have minimal benefit for primary prevention for middle-aged men who have multiple risk factors for heart disease such as high blood pressure, obesity, or diabetes. However for all other groups of people, statins do not provide a net benefit for
primary prevention when the data for primary and secondary prevention are carefully separated.

So why did the 2004 National Cholesterol Education Program guidelines expand the previous guidelines to recommend that more people take statins (from 13 million to 40 million) and promote statins for primary prevention (or about 75% of the patients taking statins)? Could it have been that 8 of the 9 experts on the panel who developed these guidelines had financial ties to the drug industry? Thirty-four other non-industry affiliated experts sent a petition to protest the recommendations to the National Institutes of Health saying the evidence was weak. It was like having a fox guard the chicken coop.

It’s all in the spin. The spin of the statistics and numbers. And it’s easy to get confused.

When you look under the hood of the research data you find that the touted “36% reduction” means a reduction of the number of people getting heart attacks or death from 3% to 2% (or about 30-40%). It means that only 1 out of 100 people treated will receive a benefit.

And that data also show that treatment with statins only is effective for secondary prevention, in other words for those with documented coronary events. In those who DON’T have documented heart disease, there is no benefit when the primary and secondary prevention data are teased out from the large trials.

In those at high risk for heart disease about 50-100 people would need to be treated for 5 years to reduce one cardiovascular event. Just to put it in perspective if a drug works, it has a very low NTT (number needed to treat). For example, if you have a urine infection and take an antibiotic, you will get near a 100% benefit. The number needed to treat is “1”. So if you have an NTT of “50-100” like statins do for preventing heart disease in 75% of the people who take them, it is basically a crap shoot.

Yet at a cost of over $28 billion a year, 75% of all statin prescriptions are for exactly this type of unproven primary prevention. Simply applying the science over 10 years would save over $200 billion. This is just one example of reimbursed but unproven care. We need not only prevent disease but also prevent the wrong type of care.

If these medications were without side effects, then you may be able to justify the risk – but they cause myopathy (even in the absence of pain and elevated CPK), sexual dysfunction, liver and nerve damage and other problems in 10-15% of patients who take them.

If lowering cholesterol is not the great panacea that we thought, how do we prevent and treat heart disease.

If lipids are implicated in the development of atherosclerosis, then is the right question “how low is the LDL target level?” Could it be that the right question is “what causes lipids to become atherogenic and how do we treat that?” Conventional methods of lipid analysis are outdated.
because we now understand that atherogenic particles are small dense HDL and LDL and large VLDL particles. Insulin resistance, oxidative stress and inflammation cause this atherogenic lipid phenotype, and while statins may lower inflammation marginally, they do not have significant effect on increasing lipid particle size.

It is lifestyle changes including a low glycemic load diet and exercise that lowers atherogenic lipid particles, oxidative stress and inflammation. Niacin also can increase lipid particle size and raise HDL-C and reverse atherosclerotic plaque. We use the tools we have, not necessarily the right “medicine” for the problem. The right “medicine” for heart disease is a healthy lifestyle, which works better than medication. Statin use is not without risk and the benefit is overstated, especially for it major indication – primary prevention. The question then becomes, what are the true contributors to cardiovascular disease?

Prime Contributors to Cardiovascular Disease

The interaction of genes, lifestyle, and environment determines risk. These dynamic interactions lead to the primary drivers of cardiovascular disease including insulin resistance, inflammation, oxidative stress and inflammation, environmental toxins, and stress.

The data show that preventing heart disease has very little to do with simply lowering LDL cholesterol with statins. Our current thinking about how to treat and prevent heart disease is at best misguided, and at worst harmful. We believe we are treating the causes of heart disease by lowering cholesterol, lowering blood pressure, lowering blood sugar with medication. But we are treating surrogate risk factors, not causes. The real question is what causes high cholesterol, high blood pressure and elevated glucose in the first place. It is certainly not a medication deficiency!

It is the environment influencing gene expression that determines risk. In other words, it is the way we eat, how much we exercise, how we deal with stress and the effects of environmental toxins that are the underlying causes of high cholesterol, high blood pressure and high blood sugar. That is what determines the risk of heart disease, not a lack of medication.

The research clearly shows that changing how we live is a much more powerful intervention for preventing heart disease than any medication. The “EPIC” study published in the Archives of Internal Medicine studied 23,000 people’s adherence to 4 simple behaviors (not smoking, exercising 3.5 hours a week, eating a healthy diet [fruits, vegetables, beans, whole grains, nuts, seeds, and limited amounts of meat], and maintaining a healthy weight [BMI <30]). In those adhering to these behaviors, 93% of diabetes, 81% of heart attacks, 50% of strokes, and 36% of all cancers were prevented.

And the INTERHEART study, published in The Lancet in 2004, followed 30,000 people and found that changing lifestyle could prevent at least 90% of all heart disease.
These studies are among a large evidence base documenting how lifestyle intervention is often more effective in reducing cardiovascular disease, hypertension, heart failure, stroke, cancer, diabetes, and deaths from all causes than almost any other medical intervention. It is because lifestyle doesn’t only reduce risk factors such as high blood pressure, blood sugar, or cholesterol. Our lifestyle and environment influence the fundamental causes and biological mechanisms leading to disease: changes in gene expression, which modulate inflammation, oxidative stress, and metabolic dysfunction. Those are the real reasons for cardiovascular disease, not a statin deficiency.

Ignoring or giving lip service to the underlying causes and treating only risk factors is somewhat like mopping up the floor around an overflowing sink instead of turning off the faucet, which is why medications usually have to be taken for a lifetime. When the underlying lifestyle causes are addressed, patients often are able to stop taking medication and avoid surgery.

Cholesterol is only one of many factors that lead to cardiovascular disease, and it may not even be the most important one. Inflammation and insulin resistance are much more important and these are driven by what we eat, now much we exercise, how we deal with stress and our body burden of environmental toxins. We focus on cholesterol because it is the factor for which we have best medication. But remember if all you have is a hammer, then everything looks like a nail.

A comprehensive approach to treating the system, not the symptom using diet changes, based on a whole food, plant based diet rich in omega 3 fats, antioxidants and phytonutrients, supplements, exercise, and strategies for treating chronic low level environmental toxicity can have a dramatic impact the risk of heart disease. And there is a good side effect--this approach reduces the risk of nearly all chronic diseases.

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\[\text{iv IBID}\]
\[\text{vi Hansson GK Inflammation, Atherosclerosis, and Coronary Artery Disease N Engl J Med 352:1685, April 21, 2005}\]
\[\text{viii Mora S, Ridker PM. Justification for the Use of Statins in Primary Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER)--can C-reactive protein be used to target statin therapy in primary prevention? Am J Cardiol. 2006 Jan 16;97(2A):33A-41A.}\]


