From the JUPITER Crestor study: competing hypotheses,
life-style changes, and potent compounds available in our foods,
to an opportunity for health-care reform
and many other reforms needed in the US

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For Dr. Majid Ali, WBAI, March 9, 2009

Part 1. The JUPITER Crestor study: competing hypotheses

What brings us together today? [1]

Ah, last November we got the results of the JUPITER Crestor study, a study that was led by medical researchers at Boston's Brigham & Women's Hospital.

What did the JUPITER Crestor study test? [1]

Here is the stated hypothesis: "we hypothesized that people with elevated high-sensitivity C-reactive protein levels but without hyperlipidemia might benefit from statin treatment."

What is "C-reactive protein (CRP)"?

Elevated CRP is an indicator of inflammation in arteries that suggests patients may be prone to catastrophic blood clots.

What does "without hyperlipidemia" mean?

"Without hyperlipidemia" is used to mean "without a high measured level of total cholesterol".

What are "statins"? [2]

Statins are a class of drugs that inhibit an enzyme in the liver (HMG-CoA reductase), which results in
-- decreased cholesterol synthesis,
-- increased synthesis of LDL receptors, and
-- an increased clearance of low-density lipoprotein (LDL) from the bloodstream.

Once you start taking statins daily, the first results can be seen after one week of use and the effect is maximal after four to six weeks.

OK, this benefit is maximal within weeks, it doesn't take months or years.

What did the authors of the JUPITER Crestor study conclude?

There are of course many statements in their Conclusion, but here is the statement that most directly relates to their hypothesis:

> "In this trial of apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events."[1]

That certainly sounds like good news.

What was reported in the press?

Here is what health writer Stephen Smith of the Boston Globe reported: [3]

1. Patients had a high CRP but healthy cholesterol readings.
2. A test group was given a 20 milligram dose of rosuvastatin each day.
3. The test group suffered 31 heart attacks and 33 strokes, compared with 68 heart attacks and 64 strokes for the placebo group.
4. The only serious side effect was diabetes.
5. 25 people would need to take the statin for five years to prevent one serious cardiovascular episode. [cost: $150,000]

Ah hah, so as we analyze competing hypotheses about this study, costs and diabetes may be important.

What questions did I email to Dr. Majid Ali? [4]

1. What life-style changes can cut our stroke and heart attack rates without statins' risks of diabetes and their high costs? How about:
    1. Avoid drinking chlorinated water. It inflames the arteries.
    2. Avoid drinking water with low pH. Acidity and inflammation go together.
    3. Floss teeth and dribble hydrogen peroxide on toothbrush. Gum bacteria leaking into the blood stream causes agglutination of red blood cells.
    4. Take B vitamins. They lower homocysteine.
    5. Take an occasional aspirin. It fights coagulation of red blood cells.

2. If life-style changes like these make the arteries less inflamed and the blood less agglutinating, wouldn't they be a cheaper and less risky alternative to statins?

What was Dr. Ali's response? [5]

1. Would you like to join me on WBAI to explore the crucial question you raise?
2. We will talk about your sense of the health problems we face with focus on cholesterol or other subjects of your interest.
3. I include the manuscript of my paper, which will be published in March, 2009, for your interest. Please feel free to use part of this article to illustrate your points, if you wish. [6]

I will include extensive quotes from Dr Ali's paper in this analysis.

Who am I to bother raising health care questions with Dr. Ali?

1. Professionally, I have years of experience in bio-medical engineering:
   1. I have patents in ROI-finding for digital radiographs,
   2. My ECG filter has been used in Siemens' cardiac MR devices,
   3. I developed an ECG triggering algorithm for cardiac MR,
   4. I developed a sensing function for cardioverter-defibrillators, and
   5. I led a group that worked on premature ventricular beat detection for patient bedside monitors.

In addition,
2. personally, like Dr. Ali, I think science-based decisions about my life-style can do a lot to keep me in best health.

What happened when I emailed the same questions to health reporter Stephen Smith of the Boston Globe?

Stephen replied: [7]

> "From the Great Minds Category: Just this Monday, in our weekly Health/Science section, I wrote a follow-up piece exploring non-pharma approaches to reducing CRP."

Ah hah, so Stephen was asking questions about alternatives too.

What was in Stephen's article about non-pharma approaches? [8]

1. Stephen quoted the lead researcher of the JUPITER study, Dr. Paul Ridker, who himself said:

> "The first, second, third, and fourth intervention for anyone with elevated CRP is (1) get to the gym, (2) lose a few pounds, (3) throw away the cigarettes, and (4) start thinking about a healthier diet. That remains overwhelmingly the most important intervention for lowering cardiovascular risk."

Obviously, no statins are necessary for these first four interventions.

Plus, Steve's article specifically mentioned:

2. A UMass study in 2006 showed that people with fiber-laden diets were 63 percent less likely to have inflammation problems.

So, Steve's article quotes the lead JUPITER doctor as saying statins are way down the ordered list of things you should do for elevated CRP. In particular, statins are below doing something about a healthier diet.

Did the Ridker/Brigham study itself make any mention of these first, second, third or fourth recommendations of Dr. Ridker?

No it did not. The word diet, for example, does not appear in the study report.[1]

To be fair, however, diet was not a controlled experimental variable in the JUPITER study, and by staying focused on those variables that were controlled one tends not to venture into discussion about other variables that might or might not be related, closely or remotely.

What are the questions that I raised for Dr. Ali at this point?[9]

1. Should we mention these four recommendations from Dr. Ridker if we explore the question of life-style changes to cut the risk of heart attack and stroke?
2. Should we think of statins as a short-term tactic for suppression of inflammation?
3. Should we think of life-style changes as a long-term strategy for prevention of inflammation?

In my mind, worrying about tactics is like asking the question: given that we've gone to war, how can I avoid getting shot?

On the other hand, strategy is somewhat like asking the question: how can I minimize the chance that we go to war in the first place?

Who else was discussing the JUPITER study at this time?

Many people. [3,10,11,12,13]

1. Study participant Matthew Mintz said: [10,11]
   1. "It will likely change guidelines"
   2. "If you are a man over 50 or a woman over 60, you should definitely ask your doctor to check your CRP if your cholesterol is relatively normal. If your CRP is elevated, I think Crestor 20mg is a good option, since it is not clear that other medications (specifically simvastatin) would provide similar benefit."

I was thinking: other medications? What about life-style choices?

   3. "What about diabetes? There is no biologically plausible reason to suspect Crestor as a cause of diabetes. However, both groups had a 41% prevalence of metabolic syndrome, which is a pre-diabetic state. Thus, it is not surprising to find an increase in diabetes in both groups."

We will have a lot more to say about Crestor and diabetes below.

2. Jaan Sidorov predicted an explosion in statin use, especially: [10]
   "among persons that would not have otherwise qualified for treatment."

Oh ho, must I now "qualify" for treatment? Am I supposed to wish that I were "qualified" for treatment?

3. Merrill Goozner commented and was skeptical, asking whether CRPs and Crestor will be the next chapter in medical waste.[10]

OK, a wasteful approach could be a problem to watch out for.

4. Cardiologist Dr. Wes said:[10]
"If we assume that a 20-mg daily rosuvastatin (Crestor) tablet costs $107 per month to treat the average patient, and that twenty five patients have to be treated for five years to prevent one cardiovascular complication (and this does not include the annual liver function tests, the cholesterol tests, the C-reactive protein checks, etc), we begin to focus on an inevitable realization: that prevention is a remarkably expensive way to deal with our exploding health care costs."

Wouldn't we rather say that prevention **via Crestor** would be a remarkably expensive way? Aren't there other options for prevention?

5. Maggie Mahar said:[10,12]
1. Would you want to take this drug for the rest of your life based on the possibility that you might be the 1 out of 120 who benefits?
She answered "it depends":
The patients who took Crestor showed "significantly higher
1. glycated hemoglobin levels and
2. incidence of diabetes".

So, Maggie brings up hemoglobin problems as well as diabetes problems.

6. Dr. Gregg Fonarow of UCLA said: [3]
"This really changes everything", when doctors encounter patients in their 50s, 60s, or older, they should "make sure
1. there are absolutely no risk factors present and
2. no elevation of CRP before deciding it's safe for that person to leave without a statin prescription."

Was anybody else discussing JUPITER at the time?

Yes, Dr Richard Fogoros, who writes on the web as "DrRich" made extensive comments. Here is what he said:[13]

1. "This study is noteworthy because it is the first large randomized trial to show that Crestor (or any statin) can markedly reduce the incidence of some very nasty cardiovascular outcomes in people who are considered to have 'normal' cholesterol levels."

Well that sounds good, but what else does he say?

2. "But, as with any clinical trial, this one does not answer all the questions that we would like to have answered."

It is natural to ask at this point is DrRich being super-fussy? The JUPITER results speak for themselves. How important can "all the questions" be?

Here are DrRich's four questions:[13]

1. "This trial, for instance, does not tell us whether the beneficial

outcome is specific to Crestor, or is a class effect of all statins: DrRich believes it is very likely to be a class effect, 'since the statins all tend to behave similarly in virtually every other way.'"

So, if we get to a point where using drugs is appropriate, are there less expensive alternatives to Crestor?

2. "This trial does not tell us whether reducing CRP levels is beneficial - it only tells us that giving Crestor to people with high CRP levels is beneficial":
If statins are best thought of as "plaque-stabilizing drugs instead of cholesterol-lowering drugs, their benefit may not rely on lowering either CRP or cholesterol."

I think this point is an important one. Not adding a loose surface to the plaque may be a benefit, whether or not a CRP or cholesterol measurement is reduced.

3. This trial "does not tell us whether using CRP as a screening tool is actually helpful":
"Only patients whose CRP was elevated were enrolled in this study."
The selected patients "tended to be overweight, to have a fairly high incidence of metabolic syndrome and to have a relatively high incidence of smoking." Similar patients "with normal CRP levels might have had the same outcome": a lowering of heart attack and stroke.

Perhaps requiring elevated CRP screens out most of the people with metabolic syndrome, most of whom could have benefited.

4. "This trial does not tell us the risks of lifelong Crestor therapy. Statins have been in widespread clinical use for nearly 20 years. One may think it unlikely that they hold very many surprises at this point", but perhaps Crestor is not like other statins.

If Crestor is not like other statins, among the differences there could be ones that cause problems. If Crestor is like other statins, why would we want to pay for the most expensive statin on the planet?

These questions seem serious.

Next, DrRich imagines what would happen, as he says, **"if medicine were practiced the way it ought to be"**: [13]

1. "the doctor would discuss the pros and cons of statin therapy - the risks, the potential benefits, and all the quite important unknowns."
2. "At the end of the day,
   1. some patients would insist on avoiding drug therapy at all costs;
   2. others would insist on Crestor and nothing else;
   3. yet others would choose to try a much cheaper generic statin; and
   4. some would even opt for a trial of lifestyle changes before deciding on statin therapy."

Good, others are mentioning life-style changes too!

Now the other shoe drops: "**But**", says DrRich, "**we don't practice medicine the way it ought to be**":
1. "We practice it according to guidelines."
2. "And this makes the stakes very high when it comes to a clinical trial like JUPITER."

Why is guidelines-based treatment "high-stakes" in this case?

Because as DrRich says "guidelines do not generally permit a range of actions tailored to fit individual patients - they generally present a binary answer. In this case, the binary answer yields either
1. no change in clinical practice (and no change in spending), or
2. a change in clinical practice (and an increase in spending, on Crestor, amounting to several billion dollars a year)."

So, what is DrRich's conclusion about the JUPITER trial? [13]

1. "The results of the JUPITER trial are striking and important but incomplete, and ought to change the conversation between, but not dictate the actions of, doctors and patients".

2. "Those who want to change the guidelines ... have painted themselves into a corner... They will not be able to say, for instance, "Statins are pretty much alike, so we'll make the guidelines say 'statins' instead of 'Crestor.'" For JUPITER did not study 'statins,' it studied only Crestor, the most expensive statin on the planet."

3. "Our total capitulation to the dictates of evidence-based medicine means that companies must fund large, expensive clinical trials before they are allowed to sell a new product, or create a new indication for an old product. This evidence-based paradigm is inherently a double-edged sword:
   1. It creates a huge barrier to the development and adoption of expensive new therapies (which is a "covert rationing" dividend of evidence-based medicine), but
   2. it also creates opportunities, for companies who manage to successfully complete such trials, to create iron-clad indications for their products. For, once a product has been "proven" in a randomized clinical trial, there is no easy way to legitimately keep that product out of the guidelines and off the shelves. The makers of Crestor have simply figured out the rules.

4. Unfortunately, the only legitimate way to turn aside the results of a costly but statistically definitive, evidence-based study is by rationing healthcare.

5. If we decide that a drug does some good, then we'll need to link that "good" to a procedure that measures whether the "good" is worth

the money we would need to spend to achieve it."

I might insert at this point that we should ask about pursuing life-style changes that we can well afford.

But let us allow DrRich to finish his line of thought. He says: [13]

1. "The only real reason there is any controversy is because of the cost of Crestor.
2. That cost is what makes us want to withhold Crestor, the high cost makes us want to ration Crestor.
3. If we were rationing healthcare openly, then we could do an objective, full-bore cost-benefit analysis taking into account
   a. the cost of the drug, as well as
   b. the cost that would be incurred by failing to stop preventable heart attacks, strokes, etc.:
   1. We would determine where the overall cost-benefit result fell within our coverage criteria.
   2. If [Crestor] met the criteria we would cover it, if not, not.
4. But we insist on doing our rationing covertly, our covert rationing paradigm is simply another demonstration of Corollary Four of the Grand Unification Theory of Healthcare: Covert rationing corrupts everything it touches."

OK, DrRich drove his comments
-- from questions that remain unanswered by the Jupitor study,
-- to costs, and toward what he calls "the corruption of covert rationing."

DrRich also makes a technical point that is worth noting: [13]

1. Longitudinal analysis shows that the risks of heart attack and stroke increase over time.
2. At 4 years in the JUPITER study, the placebo group can be estimated to have roughly an 8% event rate, compared to roughly a 3% event rate for the Crestor group.
3. This analysis yields a benefit higher than that quoted by Steve Smith, which was derived from an editorial summary by Dr. Mark Hlatky.

I think DrRich's comments are very helpful. I agree there is controversy about this study given the cost of Crestor. But I also think there is controversy about this study beyond the cost of Crestor.

I think there is controversy about the long-term health benefit of taking this drug, because, for example, of the elevated glycated hemoglobin levels and incidence of diabetes.

In that regard, it was wonderful to receive Dr Majid Ali's comments about this study.

What were Dr. Majid Ali's comments about the Crestor study? [6]

Here, under several headings, are important comments from Dr. Ali.

IS LOW BLOOD CHOLESTEROL LINKED TO MANY DISEASES? [6]

1. Low blood cholesterol levels have been linked with multiple sclerosis, Parkinson's disease, Alzheimer's disease, and several psychiatric disorders. What doctors, in their right minds, will give Crestor to healthy subjects with normal cholesterol levels?

This question presumably becomes more important the longer one takes Crestor. So we have a "related rates" problem: does the rate at which heart attack and stroke decrease more than compensate for the rate at which other problems increase?

We are also led back to the question of alternatives: are there treatment or life-style alternatives that reduce heart attack and stroke AND that don't have the bad side effects of lowering a person's normal cholestorol?

IS THERE A CONNECTION BETWEEN LOW BLOOD CHOLESTEROL AND DIABETES? [6]

2. Crestor blocks the enzyme HMG co-reductase, which is essential for cholesterol synthesis, so by definition this study disrupted cholesterol metabolism in 9,000 apparently healthy people.

   The human body produces vitamin D from cholesterol, so we would expect Crestor to alter vitamin D metabolism. Some patients who take statin drugs continously show abnormally low vitamin D levels despite daily vitamin D supplementation in doses of 1,000 to 2,000 units.

OK, here is a specific example of why any downside of taking Crestor may become more and more important the longer one takes it.

   Disturbance in vitamin D metabolism leads to disturbances in the metabolism of calcium, phosphorus, and the parathyroid glands, so we would expect Crestor to disrupt those aspects of metabolism.

OK, Crestor's disturbance of vitamin D metabolism may lead us to other metabolic disturbances.

   Since vitamin D is essential for keeping the inflammatory and immune responses within physiological limits, we would expect Crestor to interfere with these essential aspects of health.

Ah hah, here is a relation between vitamin D and inflammation. We may now be thinking that in the JUPITER study Crestor was treating a symptom but not the cause. Still, if Crestor can quickly treat the symptom but one can only slowly treat the cause, there might be a place for Crestor, e.g. in the short-term.

   Calcium, phosphorus, the parathyroid glands, and the inflammatory and immune responses play crucial roles in preserving diverse functionalities of cell membranes, so we would expect Crestor to interfere with the functions of all cell receptors (including the insulin receptor) embedded in the cell membrane.

Ah hah, Crestor interferes with insulin receptors. Dr Ali is on the way to explaining the induced diabetes.

> Since insulin cannot work without functioning insulin receptors, we would expect Crestor to cause insulin resistance, hyperinsulinemia (excess insulin in the blood), and high blood sugar levels (since insulin cannot transfer glucose into the cells for utilization).

OK, Crestor may cause high blood sugar levels.

> A growing body of clinical and experimental evidence links vitamin D deficiency with a higher incidence of diabetes; the diabetic status improves with vitamin D supplementation.

So, should those who take Crestor also take vitamin D supplements? No, it might not work! Dr Ali already noted above that some patients who take statin drugs continously show abnormally low vitamin D levels despite daily vitamin D supplementation in doses of 1,000 to 2,000 units. Not good.

> The best diagnostic test for diabetes is the blood's A1C value, which is raised by high blood sugar levels, so we would expect Crestor to cause elevated blood A1C, i.e. to cause an indication of diabetes, in a large number of healthy people who are given Crestor.

So, although Dr. Mintz may have overlooked this relationship, Dr. Ali proposes a very specific connection between Crestor and diabetes:

Take Crestor, lower the cholesterol, lower the vitamin D, raise the insulin resistance, raise the blood sugar level, raise the blood A1C value, and voilà, by definition you have diabetes.

By trying to reduce one problem, the risk of heart attack or stroke, we may create another problem, diabetes. We should think about alternatives.

Note however, that ever since the MRC Heart Protection Study, statins are indicated even for diabetics, provided these patients are at sufficiently high risk of major vascular events, and irrespective of their initial cholesterol concentrations.[14]

Again, we should think about alternatives.

HOW MUCH DIABETES SHOULD BE CAUSED BY LONG_TERM TREATMENT WITH CRESTOR? [6]

> 3. One goal of the trial was to lower LDL cholesterol levels to about 55 mg/dL. What are the long-term consequences of lowering LDL cholesterol to 55 mg/dL? We do not know. The Jupiter trial was terminated after an average duration of 19 months. Terminating the trial made sure that no one would find the full extent of the adverse negative effects of Crestor.

So, the observed side effect of diabetes is bad and the full extent of it may be worse. I am more interested than ever in alternatives to treatment by Crestor.

SHOULD WE EDUCATE FOR USE OF NATURAL ANTI-INFLAMMATORY MEASURES? [6]

4. How many of those healthy people could have been saved from diabetes if the same amount of money was spent to use natural anti-inflammatory measures to normalize the blood levels of C-reactive protein?

Go on. I want to hear more.

> Sixty million dollars can buy an enormous amount of authentic health education for the people. They can be taught how to reduce inflammation in the body - how to normalize the minimally raised blood levels of C-reactive proteins, among many other benefits - with natural, nondrug measures, such as free Limbic Breathing and Limbic Exercise, sugar restriction, hydrogen peroxide foot soaks, castor oil rubs, turmeric, and ginger.

Dr. Ali wants us to think of exercise and diet first? Why, that's what Dr. Ridker of the JUPITER study eventually said too!

ARE THERE FURTHER DISCONCERTING FACTS ABOUT THE JUPITER STUDY? [6]

5. In our thoroughly corrupt system of conducting trials, doctors paid by drug companies fudge data and the companies regularly deceive the medical profession by hiding negative data. This system will never allocate sufficient funds for education by integrative physicians who refuse to take money from any companies.

Ouch! However, if we dismiss this impolite or shocking comment, we may be dismissing the possibility that physicians working with the drug companies impose a kind of self-deception on themselves, and are overcome by a narrow focus, and by enthousiasm for a result within that focus. I do not think we want to allow ourselves to be shocked.

Indeed Dr. Ali has anticipated our shock. He puts his shocking comment in larger context by quoting a former editor-in-chief of the New England Journal of Medicine. Here is Dr. Jerome Kassirer:

> Some physicians become known as whores. "Whore" is a strong descriptor, but I heard it repeatedly from colleagues about physicians who tour the country for drug companies, changing their talks repeatedly to hawk the products of the company that is sponsoring their visits.

Okay, we may have a possible problem of recruitment here: the association with a drug company may recruit the physician into a particular bias.

What other disconcerting facts does Dr. Ali see?

6. All statin drugs cause liver toxicity, fatigue, and increase the risk of cancer. The company [AstraZeneca] claimed Crestor did not cause toxic effects any more than the placebo drug. But a cursory look at the Crestor entry in the Physicians' Desk Reference carries a

long list of adverse effects.

So, how is it that all 9,000 people who were given Crestor for a median duration of 19 months in this trial were immune to the drug toxicity. Was the placebo pill used by the company just as toxic as Crestor? Reality check: All earlier statin trials reported adverse effects. For instance, on December 21, 2007, The New York Times reported a 19 percent rate of adverse effects of Zetia with Zocor, a statin drug.

Yes, toxicity with statins is a disconcerting fact.

7. There were approximately 1.5 percent more smokers in the placebo group than in the Crestor group.

OK, the experimental groups were somewhat unbalanced. That's bad. And in a direction that increases the apparent benefit of Crestor.

8. There were roughly five percent more people with a family history of congestive heart failure in the placebo group than in the Crestor group.

Here is another imbalance that increases the apparent benefit of Crestor.

9. 40% of [the 18000] people [who served as jubjects in the experiment] had features of metabolic syndrome. So, many of the "healthy" people in the study were actually not healthy.

The phrase "metabolic syndrome" is not always used in a well-defined way but here it probably means that there was already a group of risk factors present for heart disease, stroke and diabetes, including perhaps "syndrome X or insulin resistance syndrome" and possibly depression.[15]

10. An editorial about the Jupiter trial clarified that the company screened 89,890 subjects to select the 17,802 chosen to be included in the trial. The devil is in the detail. What did the company know about the 72,088 people left out of the trial?

Perhaps the Company knew nothing about the people left out of the trial, but it would not hurt to know the answer to this question.

11. At the time of the termination of the study -- median duration of only 19 months rather than the planned four years -- only 75 percent of participants were taking the pill. How many of them dropped it because of adverse effects? The company chose not to disclose that information.

Why was only 75% of the test group taking Crestor at the end of the trial? OK, this too is a serious question.

Where do all these results and interpretations leave us?

I see three competing hypotheses here:

1. WE SHOULD ACT: We should change the guidelines, and be glad we can do something more to help our patients. Advocates are Drs. Ridker and Mintz.

2. IF WE PRACTICED MEDICINE LIKE WE SHOULD, WE WOULD CONSIDER ALTERNATIVES TO STATINS FIRST: As DrRich says: The really interesting question now is whether CRP (and for that matter, cholesterol) really are "bad" blood products that need to be lowered with statins (which seems to be the mainstream point of view), or instead whether statins are chiefly plaque-stabilizers that will improve the outcome of people with plaques - however you choose to intuit their presence. Advocates are Dr. Fogoros, and also, eventually, Dr. Ridker.

3. WE SHOULD EDUCATE SPECIFICALLY FOR THE USE OF NATURAL ALTERNATIVES: For reasons that include everything from the connection of rosuvastatin (Crestor) to diabetes to the many ways in which this experiment is less than what it may seem or what we need, we should educate for the use of alternative, "natural" methods. Advocate is Dr. Ali.

Are these three competing hypotheses mutually incompatible?

Not necessarily. We could change the guidelines, putting statin treatment in the list of recommendations after other steps like life-style changes, and consider "natural" methods among the life-style changes.

Having explored in **Part 1** this recent "Jupiter" study which showed that the statin drug Crestor cut the risk of stroke and heart attack for people with normal cholestorol but elevated CRP, we will now explore

Part 2. life-style changes to consider before statins,
Part 3. potent and relevant compounds that we can simply choose to ingest, in so-called "food", and
Part 4. an opportunity in education for health in the US.

Part 2. Life-style changes to consider before statins,

What life-style changes might we consider before statins?

I personally do not want to get to the point where I have elevated CRP or a risk of blood clots. I personally do the following:

1. I avoid drinking chlorinated water. It inflames the arteries. [16,17]

There is a very interesting monograph on this topic by Dr. Joseph Price.[17] He induced massive atherosclerotic plaque in chickens simply by giving them one teaspoon of chlorine per quart of well-water. I let tap water stand in a pitcher so the chlorine can evaporate, then I drink it.

2. I avoid drinking water with low pH. Acidity and inflammation go together. [18]

I avoid drinking water that has been passed through filters that take out the minerals and lower the pH. Lowering the pH means making the water acid. I discovered one day that our filtered water was too acid to use in our fish tank! Acidity causes the body to steal base minerals from wherever they're available and dump them into the blood to maintain high blood pH (7.4 I believe?). Chronic acidity is associated with inflammatory, auto-immune disease.

3. I floss my teeth, use a toothpaste with baking soda and hydrogen peroxide in it, dribble extra hydrogen peroxide on my toothbrush, and dunk the toothbrush in more baking soda before brushing. [19]

Gum bacteria leaking into the blood stream causes agglutination of red blood cells. The teeth and gums are a major source of bacteria that cause red-blood cells to agglutinate. Spiking release of bacteria is why antibiotics may be recommended before tooth cleaning. Chronic release from gum disease is a risk factor for heart attack.

4. I take B vitamins. They lower homocysteine. [20,21]

Too much homocysteine is related to higher heart disease. My thanks to Dr. Kilmer McCully for pointing the way on this.

Note that the US FDA no longer allows us to take all natural forms of vitamin B6.[22,23] Pyrodoxamine is a form of vitamin B6 that occurs in fish, chicken and other foods, but, responding apparently to a petition filed by a drug company, the FDA has started treating pyridoxamine like "a new drug." Now, any nutritional supplements containing pyridoxamine will be considered adulterated and illegal, and the FDA may raid vitamin companies and seize such products.

5. I take an occasional aspirin. It fights coagulation of red blood cells.[24]

Aspirin is widely used to prevent the hyper-aggregation of platelets by divers who can tolerate its side-effects.

There may well be better references in support of these personal choices I have made, but I quickly found these.

Have I seen any benefits of my life-style changes?

Yes. When I was younger I had lypomas that were growing and growing. I had to have them operated out. My father had a lot of lypomas and he died at 53 of liver disease. Then I changed my diet and I have not had to have a lypoma operated out in 20 years. I am now 62.

I also have not had a canker sore since I started daily flossing and dribbling extra H2O2 and baking soda on my toothbrush. I have very little plaque on my teeth. After a long hiatus - 7 years -

I went back to my dentist recently, because a hidden bone in a sandwich broke off a little corner of a tooth.

The dentist said "Have you been going to somebody else?" I said, "No, Larry, I've been faithful!" He said "I'm not going to touch that mouth of yours until we do x-rays." So he got x-rays and then he said "You've been living right..."

This attention to dental health may seem a small thing but there is both a chronic and an acute aspect to it for cardio-vascular health. The chronic aspect is backeria leaking from the gums into the blood stream and causing inflammation. Are you thinking about elevated CRP?

The acute aspect is the well-known syndrome of getting your teeth cleaned, after which the spike of released bacteria into the capillaries of the gums causes a major agglutination of red-blood cells, and you end up in the hospital with a heart-attack.[25]

This attention to dental health is serious. I do not recommend not going to the dentist for 7 years like I did, but I am very happy with my daily flossing and brushing with added H202 and baking soda on the brush. I do not swallow the H2O2 of course.

Part 3. Potent and relevant compounds that we can simply choose to ingest, in so-called "food".

Now let us consider the cost and health benefits of good diet choices before allowing ourselves to be driven to statins.

Why is cost a factor in discussing our diet choices before taking Crestor? Why don't we just move directly to good diet choices?

Because I personally don't like paying much more for compounds in drugs if I could pay much less and get the same benefit from food.

In addition, we may also note that President Obama thinks the high cost of health-care is crowding out other needs from the federal budget. So as a country, the US is focusing on health-care cost.[26]

So, let's talk about the estimated cost of taking Crestor.

The estimated cost of taking Crestor, $107 per month, may not seem like a lot. It is a little more than $3 per day, possibly to save my life. Maybe I should think "I can afford it and I should do it".

Imagine that we go to the AstraZeneca "grocery store" and here is this compound, rosuvastatin or "Crestor". We know from the Crestor study that it is potent, but now we look at the price.

Fortunately, in our imagined AstaZeneca "grocery store" the price per pound can be calculated and printed for all to see on the label on the shelf.

We start to calculate the price of Crestor per pound by multiplying the 20mg per day times 30.4375 days / month which means we would be taking in 608.75 mg / month or about 0.6 grams / month.

Next, we connect the grams per month to the estimated price per month of $107, as per Dr Wes' comment above. If we are ingesting 0.6 grams per month at 107 dollars per month the months cancel and the price is $175.77 / gram.

Now, how many grams are there in a pound? Well, a kilogram is about 2.2 pounds so a little less than 500 grams is going to be 1.0 pound.

The exact number is 454.54 grams per pound.

So, if the price is $175.77 / gram and there are 454.54 grams per pound, that means AstraZeneca wants to sell us Crestor at $79,895.45 / pound.

Did you get that**? In round figures, the estimated price of Crestor is $80,000.00 / pound!**

Now, if you or your health-care program went to the AstraZeneca grocery store and they had something to ingest that costs $80,000.00 per pound, would you, or they, just -- buy it?

You may think that it must be very expensive to manufacture a statin that provides health benefits like Crestor. But not necessarily!

You could use foodstuffs known as "yeast" and "rice" to make lovastatin for example. As the Chinese have shown, taking lovastatin can cause 40-50 percent reductions in heart attacks for some populations, just as the rosuvastatin of Crestor does. [27]

I do not know if it is legal to make your own lovastatin in the US, but if it is, here is all you would need to do. Buy some yeast, called "Monascus purpureus", and some polished rice. Cost? A few dollars.

Then soak the rice in water. You can steam and sterilize the rice too if you want. Then mix in the yeast and leave the yeast plus rice to ferment at room temperature for 3-6 days, like you were making yogurt.

The result is purple rice called "red yeast rice". China is the world's largest producer of it.[27]

Once you dry and powder your red yeast rice, you can consume most of it, and save part for starter to make your next batch.

If you picked the right strain of yeast, the powdered red yeast rice will have densities of lovastatin that permit a very measurable lowering of your cholesterol.[28]

And you will have spent dollars per pound, not tens of thousands of dollars per pound.

However, I have to tell you that in 1998, the FDA banned a product (Cholestin) which contained red yeast rice extract which itself contained lovastatin.

A U.S. district court in Utah allowed the product to be sold without restriction, but this decision was reversed on appeal.[29]

As this example shows**, the cost-benefit of relying on potent compounds in foodstuffs** like yeast and rice **could be very substantial.** These compounds may be every bit as potent as the products of modern pharmacology.

So, for cost reasons alone, I think we would be very unwise to be dismissive of mere "foods".

But now let us move to the other side of the food story: good diet choices. As Hippocrates is credited with saying:[30]

Let your food be your medicine, and your medicine be your food.

If we can imagine AstraZeneca as our per-unit price-marked 'grocery store', we can also imagine our food store as our pharmacy!

Do we have to be worried that the FDA will take away foods containing the compounds that I am about to mention, like they took away pyrodoxamine and the lovastatin in Cholestin? I hope not!

But just in case**, Shhhh! Psssst! Here are some other potent compounds, ones that we can still legally buy from our food store and ingest:**

1. Potent compound: pectin [31]

Pectin is important first of all for what it does to our gastro-intestinal tract. If we're going to be ingesting things, we want to make sure that our absorption and output system is working, right? Well, pectin is a soluble fiber. It soothes the gastro-intestinal tract, helping to sweep it of bile salts and remove them from the body. And that's our hook. By removing the bile salts, pectin forces the body to make more bile, which it does by ... breaking down cholesterol! So pectin also lowers cholesterol. That's right, statins are not the only compounds that lower cholesterol. But Shhh you don't have to tell the drug companies or the FDA that you are buying pectin. Just ask for ... **bananas**.

2. Potent compound: potassium [31,32]

Potassium is an electrolyte that helps to regulate heart function and also fluid balance. The regulation of heart function and fluid balance are key factors in regulating blood pressure. Studies have shown that potassium-rich foods are very effective in lowering blood pressure and protecting against heart disease and stroke. Protecting against the effects of heart disease and stroke was the whole point of the Crestor study, right? Why not protect against one of the causes? Again, don't tell the drug companies or the FDA, just ask for .. **bananas** again, or, ask for **.. romaine lettuce**.

3. Potent compound: folic acid [18,32]

Folic acid is a B vitamin that is beneficial to heart health. It is needed by the body to convert a damaging chemical called homocysteine into other benign substances. If not converted, homocysteine can directly damage blood vessels, directly increasing the risk of heart attack and stroke. You can openly buy folic acid as a supplement, but the FDA and the drug companies will have to guess what you're doing if you just ask for ... **romaine lettuce, again**.

4. Potent compound pair: beta-carotene and vitamin C [32]

Beta-carotene is a pro-vitamin A carotenoid. If we can find a way to ingest beta-carotene along with vitamin C, a wonderful thing happens. This pair of compounds works together to prevent the oxidation of cholesterol. When cholesterol becomes oxidized, it becomes sticky and starts to build up in the artery walls, forming plaques. If these plaques become too large, they can block off blood flow, or they can break off and cause a clot that triggers a heart attack or stroke. Shhh! If you want to ingest this compound pair, just ask for **.. romaine lettuce, again**! We have beaten Crestor to the punch, at the price of a head of lettuce!

5. Potent compound: phytochemical coumarins: [33]

Coumarins have been shown to be effective in cancer prevention and are capable of enhancing the activity of certain white blood cells. The point of coumarins for our discussion is especially that they lower blood pressure and tone the vascular system. It is a bonus that they are also possibly effective when used in cases of migraines. I don't know if we can buy coumarins as a separate supplement. But we can buy them in a package that also contains balanced levels of potassium and sodium. This packaged product is great for electrolyte replacement. It has also been shown that this packaged product may help to lower cholesterol and prevent cancer by improving detoxification. The name of this packaged product? Shhht, **celery**!

6. Potent compounds: plant phenolics [34]

Plant phenolics include such potent antioxidents that they are sometimes referred to as "nutra-ceutical agents", as opposed to "pharma-ceutical agents". The term "phenolics" is used either because these compounds include in their formula a hydroxyl (OH) group attached to an aromatic carbon atom in analogy to the well known chemical "phenol", or because these compounds have a chemical structure closely related to a compound having an aromatic (phenolic) hydroxyl group.

Usually plant phenolics have more than one hydroxyl group. Such "polyphenolic" compounds have a wide range of physiological properties such as being anti-oxidant, anti-mutagenic, anti-allergic, anti-cancer and anti-diabetic. Adding these compounds to human blood serum has been shown to decrease lipid peroxidation. Some of these compounds, like phloridzin, have antioxidant activity that gives cardiovascular protection similar to that of estrogens.

Generally speaking, plant phenolics have antioxidant properties, and have been shown in in-vitro and in in-vivo studies to have positive effects on the human cardio-thoracic condition. How much would we be willing to pay for these compounds, thousands of dollars per pound? In the food store, we can buy antioxident phenolics in an inexpensive package that seems remarkably resistant to bruising on the shelf. If this package can keep itself from bad oxidization, maybe it can help keep us from bad oxidation too. The name of this package? **Granny Smiths**!

7. Potent compound: resveratrol [35,36]

Resveratrol has been shown to potentially inhibit the spread of a variety of viral infections, from influenza to HIV. It has been shown to prevent the continued reproduction of the flu virus if taken within six hours of infection.

Resveratrol has been shown to be successful in improving the health of organs, even in the face of a high calorie diet. Mice fed a high-fat diet plus 22 mg/kg resveratrol had a 30% lower risk of death than mice on the high-fat diet alone. Importantly for our discussion, addition of resveratrol to

the high-fat diet provided this benefit even though resveratrol apparently did not change the levels of free fatty acids and cholesterol, which were much higher than in the mice on a standard diet. While resveratrol has been shown to have beneficial effects as an anti-cancer, blood-sugar-lowerer, chelator and anti-inflammatory in animal tests, most of these results have yet to be replicated in humans.

Does resveratrol have your attention now as a potent, although not yet fully tested compound? Good! You can buy it in the food store, Shhh!, in **red grapes**.

Now, it took me some time and effort to track down science-based evidence of the potency of these compounds in food: pectin, potassium, folic acid, beta-carotene and vitamin C, phytochemical coumarins, plant phenolics and resveratrol.

I hope you will now not be dismissive of these compounds just because I also revealed that they are packaged in bananas, romaine lettuce, celery, Granny Smiths, and red grapes.

Note that I did not base my description of potent compounds and foods on mere "authority", I based it on evidence-based science.

What am I getting at now? Compare the following two dialogues:

1. Dialogue 1:
   Parent/doctor: Eat your fruits and vegetables.
   Child/patient: Why?
   Parent/doctor: Because I said so.
   Child/patient: [Yeah, right. Blow it out your...]

2. Dialogue 2:
   Parent/doctor: Eat your fruits and vegetables.
   Child/patient: Why?
   Parent/doctor: Because pectin, potassium, folic acid, beta-carotene
   and vitamin C, phytochemical coumarins, plant phenolics and resveratrol
   are in bananas, romaine lettuce, celery, Granny Smiths, and red grapes.
   Child/patient: [Gulp!]

What is the game you offer to your child or patient in the first dialogue? They can just seek to undermine your authority. All it takes is a smirk, a wise-crack or a funny face. Your authority is undermined.

What is the game you offer to your child or patient in the second dialogue? They can -- and should -- still seek to undermine you. You may have the story incomplete or wrong. But now, they will have to come up with alternative facts. Great, they have to take on serious criticism themselves.

See how to work it? The approach of dialogue 2 is an example of how to take on education for health. Which brings us to the last part of our discussion.

Part 4. An opportunity for health-care education in the US

Last Thursday, President Obama opened a White House health-care summit calling for allies and opponents to come together to overhaul the US health-care system.[26]

The President and any allies won't succeed in overhauling the US health-care system based on anybody's supposed authority. They'll get undermined by smirks, wise-cracks and funny faces, like in Dialogue 1, above.

He and his allies will have to educate the US. He has to provide science-based evidence as to why health-care reform is necessary. He and his allies could try to show that health outcomes are too low, and they could try to show that health-care costs are too high.

Suppose we could show that poor health-care rankings tend to arise in those parts of the US with poor education rankings. Would we open the door to the question: **Hmmm, do bad educations lead to bad life-style and health-care choices?**

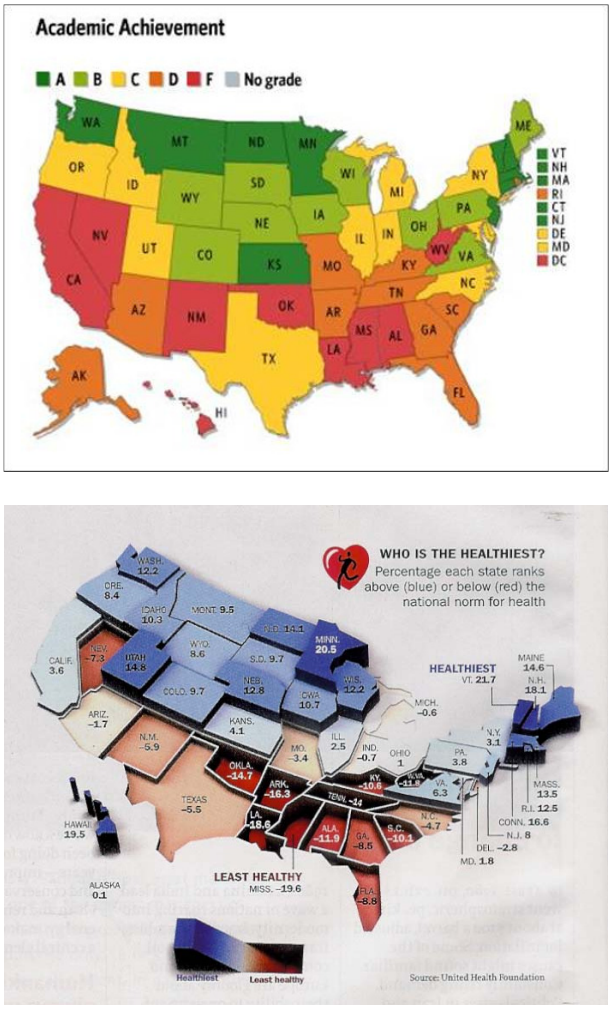

Figure 1. Statistics for 50 US states and Washington DC. Top: K-12 education rankings. Source: US Chamber of Commerce, 2007. Bottom: Health-care scores. Source: United Health Foundation, 2008, graphed by Time Magazine.

As it turns out, we can demonstrate that the lowest education rankings in the US correlate with the lowest health-care scores. Look at the above two graphics.

The top graphic illustrates the Kindergarten to 12th-grade education rankings calculated in 2007 by the US Chamber of Commerce, colored by "grade" for each state in the US plus the District of Columbia.[37] Dark-green states got A's, light-green states got B's, yellow states got C's, orange states got D's and red states got F's.

The second graphic illustrates the state-by-state public health scores calculated in 2008 by United Health Foundation and graphed by Time magazine.[38] The bluest states got the highest health scores, the reddest states got the lowest health scores.

Can you see that **the relative K-12 education rankings and public health scores are very similar**?

What does this evidence say about the effect of elementary and high-school education on the way we end up taking care of ourselves?

Does our opportunity for health-care education in the US need to be fitted into the context of a need -- and an opportunity -- for all of elementary and high-school education? I think it does.

Do we need more education by science, as opposed to education by authority, across the whole spectrum of elementary and high-school subjects? I think we do.

Having zoomed out from Crestor to health-care reform to health-care scores, we have discovered that education rankings tend to be lowest where health-care scores are lowest.

One implication is that the President and his allies will now have to look at tackling education reform in order to get to health-care reform.

Why? Because the President should be pursuing health-care reform not just to control costs but also to get better health-care results.

How are we going to get better health-care results unless people are educated enough to do what is in their best health-care interest?

Part 5. Conclusion and a broader perspective

I think we should change the medical guidelines, put statin treatment in the list of recommendations after other steps like life-style changes, and consider "natural" methods among the life-style changes, including eating potent compounds that we find in foods. But I do not understand why Crestor should cost $80,000.00 per pound.

And what about poor President Obama? We zoomed out from a problem of science-based medicine and Crestor to confront **health-care reform, and** now we see that **education reform** is necessary too, and yet**,** these **are only two of many population-based problems that the US needs to work on.**

How bad is the whole set of these population-based problems? Well, it is not up to me alone to say. Please tell me what you think.

How bad is the following set of population-based problems: besides (1) health-care, and (2) K-to-12 education, there is (3) illegal drugs, (4) violent crime, (5) homeland security, (6) retraining of unemployed adults, and (7) support for retirement. [39]

Are there other population-based problems that you would like to add to this list? How about the population-based problem of the exhausting of natural resources like oil? [39]

Only a federal government that is sufficiently representative of the US population will be sufficiently sensitive to all of these population-based problems.

To the extent that the federal government is unrepresentative of the US population, it will not be sensitive enough to these population-based problems.

I am sorry to have to report that our federal government is surprisingly unrepresentative of the US population. Do you have the time and fortitude to consider this information as well?

OK, here are some relevant questions:

1. What are the consequences of the US government downweighting the 21 most populous states so much in the selection of the US federal executive that these states' effective loss of population, 64 million people, is greater than the entire population of the rest of the country, which is only 63 million people? [39]

2. What are the consequences of the US government downweighting the 16 most populous states so much in the US Senate that these states' 68% of the US population only gets 32% of the senate vote? [39]

3. What are the consequences of the US government downweighting the 37 most populous states so much in the US constitutional amendment process that these states' 95.5% of the population can be blocked by a plurality of the remaining 4.5% of the population? [39]

4. And if these consequences are on balance bad, is there any realistic approach to a work-around? [39]

My personal answer to question 4 is that the consequences are very bad, and the campaign by National Popular Vote (www.nationalpopularvote.com) is a realistic approach to a workaround. This is of course a whole other story beyond Crestor…

Now let me try to wrap up quickly.

If you want to take narrow action to help the hearts in this country, my advice is to advocate for statins after life-style and diet changes, and only at a reasonable price.

If you want to take a broader action to help the "heart" of this country, my advice is to help National Popular Vote. That's because I think full representation of the US population via one-person one-

vote when we select the federal executive is a good first step for putting this country on a path to sufficient sensitivity to all of the population-based problems that we have mentioned.

Bottom line: the Jupiter Crestor study has led us to a pandora's box of problems which are much worse than many think, and where there is much more that we need to do. But, through action at narrow and broader scales, I am optimistic that we will be able to make a positive difference.

Thank you for your attention.

G.M. Kuhn, Ph.D.
WBAI
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