Advertising Passed Off As Research Confuses the Public

Study Published in *New England Journal of Medicine* Expands the Indications for Statins—and the Public Suffers

Today's (November 10, 2008) front page headlines worldwide announced a simple test called "highly sensitive C-reactive protein" (HS-CRP) and the most powerful cholesterol-lowering statin currently on the market, Crestor (rosuvastatin), used together, could cut the risk of heart attacks, strokes, and death from cardiovascular disease in half.[1] For the casual reader, Crestor appears to be a miracle treatment with few risks and reasonable costs. Today's publication adds to the belief of a growing number of experts that "statins are so wonderful that they should be added to our drinking water" (like fluoride).

For this study nearly 90,000 people were examined, and most of them were identified as being at increased risk for a heart attack, stroke, and/or premature death. Rather than choosing professionalism and treating the underlying causes of their health problems: their diet and lifestyle; these researchers chose commercialism; creating the most effective pharmaceutical advertising campaign ever devised. And they have succeeded.

The study was funded by the maker of the drug, AstraZeneca, and the lead author, Paul M Ridker MD, is listed as a co-inventor on patents held by Brigham and Women's Hospital related to the use of HS-CRP for the evaluation of a patient's risk of heart disease.

Profits Are Determining Medical Care

The cost of Crestor (rosuvastatin) is about $3.45 per day—much higher than that of generic statins. That amounts to $1259 a year just for this drug. Doing the math, this means to prevent one event in one "apparently healthy patient" would cost about $300,000 just for the Crestor. These figures do not include the cost of doctors' visits, the lab tests and the treatment of side effects from the medications, including the serious adverse events caused by Crestor.(Calculations: Absolute benefit of 1 event for 120 treated patients for 1.9 years at $1259 = 120 x 1.9 x $1259 = $287,052.)

Heart attacks, strokes, and the need for surgery and drugs are caused primarily by eating the Western diet, and secondarily by "bad habits," including cigarette smoking and lack of exercise. The underlying disease, atherosclerosis, is reversible. There are no side effects or added costs with diet-therapy—therein lies the problem (no profit).

How Did They Get Those Results?

1)**They stacked the deck with sick people, but passed them off as "healthy" to the press and public.** Previous studies of statins have found that people at high risk for a heart attack or stroke will benefit, but healthy people will not.[2] The deception in this study began by choosing high-risk test subjects and identifying them as "apparently healthy men and women."

The nearly 18,000 people selected for the study out of the original 89,890 screened had very high HS-CRP levels of over 4.2 mg/L. Simply based on the HS-CRP these were not "apparently healthy," but rather, people at high risk for cardiovascular disease. The cutoff value for high "bad" LDL-cholesterol level was 130 mg/dL. This allowed the inclusion of many high-risk people—"good health" is associated with a LDL below 100 mg/dL. In addition, the average blood pressure (134/80 mmHg) and total cholesterol (186 mg/dL) numbers were too high for these people to be considered "apparently healthy."

The baseline median body mass index (BMI) was 28.3 (normal 18.5-24.9), indicating most of these people were overweight or obese. At the beginning of the study 41% were reported to have "metabolic syndrome." (Metabolic syndrome is a combination of medical disorders, such as abdominal obesity, elevated blood sugar, triglycerides, and blood pressure, which considered together indicate an increased risk of

cardiovascular disease.)

2) They Emphasized Relative, Not Absolute Benefits
Reporting the "relative benefit" of a drug is the most common method used by drug companies to deceive patients and their doctors. In this case relative risk reduction was determined by dividing the number of designated events (heart attacks, stroke, and deaths from cardiovascular disease) for the treated (Crestor) group by the events for the placebo group: 83 vs. 157. This mean the treated group had half (53%) the chance of an event compared to placebo. This figure is impressive.

However, the "absolute benefit"—the real life benefit a person can expect from treatment—is a very different story. Consider the numbers: nearly 18,000 people were treated for almost 2 years. In absolute numbers this means 83/8901 or 0.9% of those people taking Crestor had a serious event, as opposed to 157/8901 or 1.8% of those in the placebo group. This is an absolute event reduction of less than 1%. In other words, 120 patients had to be treated with Crestor for 1.9 years to prevent one designated event: heart attacks, strokes, and death from cardiovascular disease.

3) Early Termination of the Study Is Impressive but Suggests Dishonesty. The study was supposed to go on for 4 years, but was stopped at 1.9 years for "ethical reasons." It was considered unethical to continue the study because continuation would mean depriving the people in the placebo group of the advantage of the treatment—Crestor in this case. "Early termination" of research is a powerful technique used by pharmaceutical companies to enhance the perceived value of the treatment in the minds of the medical profession, the press, and the public. But it has been shown that studies that are stopped early are biased and prone to exaggeration.[3] According to a recent review in the *Journal of the American Medical Association*, "RCTs (Randomized Controlled Trials) stopped early for benefit are becoming more common, often fail to adequately report relevant information about the decision to stop early, and show implausibly large treatment effects, particularly when the number of events is small. These findings suggest clinicians should view the results of such trials with skepticism."[4]

No mention was made in this report about two other recent studies (CORONA and GISSI-HF) where Crestor did not result in any improvement in survival.[5,6]

4) Researchers Underemphasized Serious Adverse Events from Crestor
One of the most important findings from this study (found in table 4) is the similar number of serious adverse events in both the Crestor-treated and placebo groups—1352 (15.2%) vs. 1377 (15.5%). How can that be? Wasn't the number of events about half (83 vs. 157) for those taking Crestor? The study focused on events (heart attacks, strokes, and deaths from cardiovascular disease) that are expected to respond favorably to treatment. The study, and the media that followed, did not give appropriate attention to all adverse events that occurred. Clearly, there was an increase in non-cardiac serious adverse events in the Crestor group. Obviously, it is not in the best interest of the sponsor of the study to give attention to this finding.

The article did mention an increase in risk of diabetes in those treated with Crestor (270 reports of diabetes, vs. 216 in the placebo group). But there must be more. Amazingly, this study reported only one case of serious muscle damage (rhabdomyolysis). The expected rate is 3.16 fatal cases per million prescriptions written for Crestor.[7] This is 16 to 80 times higher than that reported for other statins. Almost four years ago Dr. David Graham, FDA's associate director for science and medicine, named Crestor as one of five drugs that pose serious safety concerns and the FDA told AstraZeneca to pull its ads for Crestor because they do not mention its risks of causing acute kidney failure or rhabdomyolysis.

There is no long-term information on the safety of using these high doses of Crestor to lower "bad" LDL-cholesterol to 55 mg/dL (as they did in this study). This study was stopped after less than 2 years, but patients prescribed statins can expect to take them for 20 years and longer.

One More Deregulated System That Must Be Fixed

Neither the patient nor our over-burdened health care system can thrive with this kind of deception from

the pharmaceutical companies and the medical journals. Fortunately, health care professionals are beginning to recognize that what is happening in medical care is just like the tragedies we have recently witnessed in the stock market and the housing industries. Unregulated business practices lead to a few very rich people becoming even richer, and severe suffering for the rest of us. The time has come for change. Researchers and publishers must be held accountable like stockbrokers and bankers. Regulation enacted to protect the public is long overdue.

What is HS-CRP?

C-reactive protein (CRP) is a molecule produced in response to inflammation. It is non-specific, in other words, it does not identify the source of the inflammation, which could be due to an infection of a toe, arthritis, or a bad cold. The connection to cardiovascular disease (heart attacks and strokes) is that the sores (like pustules) on the artery walls cause the CRP to rise. This festering artery disease (atherosclerosis) is the underlying cause of heart attacks and strokes. The elevated CRP is simply one sign of the trouble—other signs are elevated blood pressure, blood sugar, cholesterol and triglycerides.

Highly sensitive (HS) refers to laboratory methodology used to increase accuracy. A level of less than 1mg/L indicates low risk, a level between 1 and 3mg/L indicates moderate risk, and a level greater than 3mg/L indicates high risk of active artery disease. The people in this study were **on average** in the high-risk group, in need of immediate and intensive dietary intervention.

Statins, like Crestor, are believed to be anti-inflammatory, reducing HS-CRP levels. Even without the postulated benefit of reduced inflammation, the cholesterol lowering effects of statins have been shown to reduce the risk of serious cardiovascular events in people at high risk.[2] A low-fat diet also cuts CRP in half in 4 weeks.[8] This reflects less inflammation, which means healing the arteries as a result of following a healthier diet.

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