

## **Concerned Scientists Dispute New Cholesterol-Lowering Guidelines**

### **Statin Drug Treatment Carries Great Risk, Few Benefits**

August 17, 2004, LUND, SWEDEN: Recently revised cholesterol-lowering guidelines constitute a major risk to public health according to The International Network of Cholesterol Skeptics, (THINCS), a non-profit organization of doctors, scientists and researchers.

The new guidelines, aimed at even more aggressive cholesterol lowering will result in millions more people being placed on statins. The evidence for a more aggressive treatment comes from two related trials which have been heralded as demonstrating that greater cholesterol lowering resulted in greater protection against heart disease.

These studies, PROVE-IT<sup>1</sup> and REVERSE,<sup>2</sup> were hugely flawed, and cannot be said to have proven anything. Two different drug types were given and the benefits were directly related to the drug type, and not to the degree of cholesterol lowering.<sup>3,4</sup>

THINCS' members are deeply disturbed by the ever-increasing pressure to lower blood cholesterol levels, and the underlying commercial interests that have distorted scientific research in this area. THINCS warns that statins have been excessively 'hyped' by the pharmaceutical industry and medical opinion leaders who have, unfortunately, become little more than paid advertorials.

"These drugs have been shown to produce an alarming array of side effects," states Uffe Ravnskov, MD, PhD, THINCS Chairman. "Furthermore, the public and medical profession do not realize that statins only benefit a small and select portion of the population."

Ravnskov and his colleagues worldwide point out that in the elderly, in women of all ages and in men without heart disease, cholesterol-lowering measures have not prevented a single death in any trial.

For instance, in the recent trial PROSPER,<sup>5</sup> the only statin trial that included old people exclusively, and the results of which were used as an argument for including old people for statin treatment, total mortality was unchanged, because 22 fewer deaths from heart disease and stroke was outweighed by 24 more cancer deaths. This significant increase of cancer mortality was belittled by referring to the previous trials, where according to the trial directors no increase of cancer mortality was seen. What the directors did not mention was that the mean age in these trials was about 25 years lower than in PROSPER, a crucial piece of information because cancer is mainly a disease of old age.<sup>6</sup>

It has also been ignored that in the first statin trial EXCEL, mortality was already higher among those taking statins after one year compared with the non-treated control individuals.<sup>7</sup> This trial is never mentioned in the many reviews published by those who proselytize for statin treatment and the higher mortality in the statin group was not even mentioned in the abstract of the paper.

In a recent review of cholesterol lowering drug treatment in women published in the Journal of the American Medical Association the authors concluded that "for women without

cardiovascular disease, lipid lowering does not affect total or CHD mortality” and for women with known cardiovascular disease “treatment of hyperlipidemia . . . does not affect total mortality”,<sup>8</sup> meaning of course that any decrease of heart mortality is balanced by an increased mortality from other causes.

Even in the highest male risk groups for heart disease, statin treatment resulted in 0.5 % fewer deaths per year, and this small benefit was found in the most positive of all trials. Other major statin trials, e.g. ALLHAT showed no benefit at all, a fact that has been effectively buried.

Most people probably may protest here because we have all been told that statin treatment may reduce heart mortality by between 20% and 50%. This apparent discrepancy is easily explained. For instance, the Committee mentioned that in the ASCOT trial fatal and nonfatal stroke was reduced by 27 %.<sup>9</sup> The truth is that these events were seen in about 1.7 % of the statin-treated and in about 2.4 % in the non-treated patients, an absolute difference of 0.7 percentage points. But as this small difference of 0.7 is equivalent with 27 % of 2.4 percentage points, the misleading number 27 % was used, as is usual in the trial reports wanting to potentiate the apparent benefit of treatment.

Even a small effect would of course be worthwhile provided that the treatment was free from side effects. This point is particularly important considering that aggressive cholesterol lowering may demand statin doses up to eight times higher than those used hitherto. But possible side effects are belittled by the Committee. They may have been calmed down by the trial directors, according to whom, side effects of statin treatment are rare and mild.

Obviously the Committee is unfamiliar with the scientific literature because a large number of serious side effects from statin treatment have already been published in international medical journals and/or have been reported to the American Food and Drug Administration.

Data gathered by the THINCS group show that statin drugs cause cancer both in animals and in human beings.<sup>6,10</sup> Other side effects include liver damage, nerve damage,<sup>11,12</sup> short temper,<sup>13</sup> cognitive decline<sup>14</sup> and memory loss,<sup>15</sup> and statin use during pregnancy may lead to more serious malformations than were seen after exposure to thalidomide.<sup>16,17</sup>

Best known is muscle damage. In severe cases this causes kidney failure which has claimed the lives of several hundred people thus far, and resulted in one of the worst offending statins (cerivastatin) being withdrawn from the market.

Cardiologist Peter Langsjoen notes that statin treatment may lead to heart muscle weakening and heart failure.<sup>18</sup> "It occurs because statin drugs block the production of coenzyme Q10, vital for the production of cell energy" says Langsjoen. "Evidence sent to the FDA shows marked reduction of coQ10 in patients on statin drugs."<sup>19-21</sup>

Most of the mentioned side effects were unknown when the reports from the statin trials were published, partly because in many trials a large number of people, originally selected for these trials, were excluded after a short treatment period due to non-compliance. This way of conducting a trial may result in a gross underestimation of the number and the seriousness of side effects as the reason why these patients were not compliant may have been intolerance to the drug.

All of these side effects have been seen at relatively low doses. New recommendations are to use increasingly high doses, and THINCS warn that this will result in even more complications of treatment up to, and including, death. Yet “to lower cholesterol even more is like chasing windmills”, says Ravnskov, “because any alleged benefits from statins has nothing to do with lowering LDL or cholesterol.”

This is evidently clear from two types of observations. First, the statins may provide benefit whether cholesterol is lowered a lot or only a little. It is because statin drugs have a number of effects that are beneficial to the vascular system, but their cholesterol lowering effect is not one of them.

Second, high cholesterol is not a risk factor for old people; on the contrary, many studies have shown that old people with low cholesterol run a greater risk of dying whereas those with high cholesterol live the longest.<sup>22</sup> This fact is also deemphasized by protagonists of cholesterol lowering, if it is mentioned at all, although about 90 per cent of all cardiovascular deaths occur in people above age 60. Why should cholesterol be lowered in old people if high cholesterol is associated with longevity?

The reason why high cholesterol seems to be beneficial is most probably because LDL and other lipids protect us against bacterial and viral infections.<sup>22</sup>

The Committee’s ignorance of the available literature, in particular that part which contradicts its recommendations, and their misleading way of referring to the part they are familiar with and which appears to support their stand, do not surprise us. In a rebuttal to Gary Taubes’ article *The Soft Science of Dietary Fat*, published three years ago in *Science Magazine*, the first author of the new guidelines, Professor Scott Grundy claimed that saturated fats are the main dietary cause of coronary heart disease and referred to a large number of studies. But, as we pointed out in the February 22, 2002 issue of the same journal, these studies were either not supportive, or they dealt with something else.<sup>23</sup> Unfortunately, this way of referring to the scientific literature has also been used extensively in many previous reviews from the National Heart, Lung and Blood Institute and the American Heart Association.<sup>24</sup>

"Statin drugs have been aggressively promoted by the pharmaceutical industry and medical opinion leaders," says THINCS member Paul Rosch, MD, President of the American Institute of Stress. "The new guidelines were not written by disinterested scientists, but by members of the medical community who have received major grants from the pharmaceutical industry. The recommendations are based on distorted statistical analysis of relative risk reduction that mislead doctors and the public. They are designed to turn healthy people into patients."

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