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Doing the Right Thing: Stop Worrying About Cholesterol

To the Editor:

Stamler et al¹ argue that a low cholesterol level is not the cause of the increased mortality seen in population studies but is a marker for causative factors. They are probably right, but they disregard that a high cholesterol level may also be a marker only. Smoking,² obesity,³ lack of exercise,⁴ and psychological stress,⁵ for instance, increase blood cholesterol but may cause coronary heart disease by other mechanisms.

The crucial point is that lowering cholesterol actively increases noncoronary mortality, and this increase is not balanced by a decrease of coronary mortality.^{6,7} Stamler et al¹ claim that the increased mortality found in the meta-analyses is due to selection of trials. They are wrong, because the excluded trials were mostly unrepresentative.⁸

Stamler et al¹ are skeptical of meta-analysis and use instead the results from only three trials to argue for a "healthier" level of serum cholesterol. The effects of the two largest trials were pathetic, however, and as all of them were multifactorial, their effect, if any, may have been due to other causes than cholesterol lowering.

In a recent meta-analysis of 35 cholesterol-lowering trials, mortality decreased in a subgroup of trials including 5116 individuals.⁷ But mortality increased in a much larger subgroup of 27 918 individuals. The first subgroup was called a high-risk group and the other one a low-risk group, according to the mortality of the control subjects. But how should we classify before treatment?⁹ Several trials in the so-called low-risk group were secondary preventive, and the mean cholesterol level was higher (7.15 mmol/L) than in the so-called high-risk group (6.72 mmol/L). Thus, when Stamler et al say that only those at highest risk should be treated, they impose an impossible mission on physicians. The risk is greater that we will shorten the lives of our patients instead of prolonging them.

Stamler et al¹ think that the increased mortality after drug treatment should be prevented by careful monitoring. However, I am confident that the trial directors monitored their patients carefully, probably more carefully than we physicians do, and yet mortality increased. There are also obvious methodologic problems connected with the prevention of cancer, violence, and other unexpected causes of death.

Finally, Stamler et al¹ stress the importance of diet. It is true that trials using an extreme diet or trials on patients in mental hospitals have lowered the cholesterol level significantly, but it is unrealistic to think that healthy people should accept these rigorous diets during many years. In trials where a more palatable diet was used, the effect on blood cholesterol has been trivial despite intensive counseling. In MRFIT,¹⁰ for instance, cholesterol was lowered by 2%, in the WHO study¹¹ by 1%, and in the Gothenburg trial¹² by even less. In the Helsinki study,¹³ the control group was treated by diet, but their cholesterol increased. Note also that a significant reduction of nonfatal coronary heart disease has not been achieved in dietary trials.⁸

The right thing to do is to stop the cholesterol campaign. The evidence for a causal relation among atherogenic diet, high serum cholesterol, and coronary disease is far from overwhelming. On the contrary, a host of studies have shown many inconsistencies with this idea.¹⁴⁻¹⁸

Uffe Ravnskov, MD
Lund, Sweden

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To the Editor:

Regarding the editorial in *Circulation* in October 1993, Stamler et al¹ seem to imply that the 50% reduction in coronary and cardiovascular disease death since the 1960s is significantly related to health policies, including reduced cholesterol, more physical activity, etc. In the same issue, however, Kaplan and Keil² document the increasingly apparent relation between cardiovascular disease and socioeconomic factors, including income, education, and occupation. Blue collar work, low income, lower education level, and high psychological stress relate to cardiovascular mortality. Since the 1960s, per capita income in the developed world has continued its phenomenal ascent, with the standard of living 3 times its level 60 years ago in the United States, 7 times in Germany, and 10 times in Japan. This has been accompanied by a relative reduction in blue collar jobs as well as a widespread increase in education levels. Kaplan et al cite the work of Williams et al,³ who report a 5-year survival independent of all baseline invasive and noninvasive medical prognostic factors of 0.91 for patients with coronary artery disease and an annual

household income of \$40 000 or more as compared with a 5-year survival of 0.76 in patients with incomes of \$10 000 or less.

It would seem plausible from the above that the 50% reduction in coronary and cardiovascular disease death since the 1960s in the developed world is most likely predominantly a result of the increasing wealth and accompanying lifestyle modifications resulting from this wealth rather than predominantly a result of more enlightened health policies, although such policies may well have made some contribution, as Stamler et al suggest.

G. Kessler, MD
Caesarea, Israel

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Reply

Our *Circulation* editorial emphasized that the cornerstone of US national health policy on serum cholesterol is a population-wide strategy to achieve by *dietary means* a downward shift in serum cholesterol level, first and foremost for the *primary prevention* of epidemic coronary heart disease (CHD).¹ It concluded: "The present national policy . . . has the added merit that the recommended healthier eating patterns can be beneficial in preventing or controlling other chronic diseases as well as coronary disease. There is no sound evidence that justifies a withdrawal from this policy. On the contrary, we need to expand and intensify efforts to achieve its goals."¹

Our editorial assessed as unfounded all three concerns set down in the prior editorial by Hulley et al.² In the first paragraph of their letter above, Hulley et al note this and restate the three concerns but make no effort to reply to our reasons for concluding that concerns No. 1 and No. 2 were unsound. They focus solely on concern No. 3, related to meta-analyses of data from randomized controlled trials (RCTs) of cholesterol lowering. Olson and Ravnskov also rely heavily on these meta-analyses as a basis for their critiques of our editorial and of US national policy on serum cholesterol.

Altogether, their three letters cite findings in 8 such meta-analyses (of 6 to 35 trials).³⁻¹⁰ However, the fact is that all these meta-analyses are at best irrelevant or at worst misleading in regard to recommended dietary approaches for CHD primary prevention. Specifically, of the cited unifactorial trials on CHD primary prevention, only two were dietary trials. All others were drug trials, hence by definition unrelated to the main thrust, that is, the nutritional emphasis, of US national policy. Lumping diet and drug RCTs together is a flawed use of the meta-analysis method, and citing overall findings from such meta-analyses is inappropriate when the primary issue under discussion is national nutritional policy. Moreover, combining all these RCTs results in ignoring the details of their nature, design, procedure, and outcome that are critical for assessment of their soundness and policy relevance.

As to specifics, first on the two unifactorial diet trials,^{11,12} both were actually combined primary and secondary prevention trials. Both had design features that make their findings uninformative in regard to public policy on reduction of coronary and all-cause mortality rates by population-wide improved nutrition. First, they

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U Ravnskov

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