

Does Decreasing Cholesterol Levels Increase the Death Rate from Accidents, Homicides and Suicide?

A. Hoffer, M.D., Ph.D.¹

Recently Muldoon, Manuck and Matthews (1990) concluded that decreasing cholesterol levels, either by dietary means, drugs, or a combination of both, increased the death rate from causes not related to illness. They examined the data derived from six randomized primary prevention trials on 24,847 males, mean age 47.5. For 119,000 person-years there were 1147 deaths. There was a decrease in deaths from coronary heart disease and an increase in deaths not related to illness. Two studies used diet alone, one used Clofibrate, one Colestipol and diet, and one, the sixth study, used Gemfibrozil and diet. They cautioned that programs for lowering cholesterol ought to be more careful and investigate further these possible connections, i.e. that the process of lowering cholesterol is in itself inherently risky. In their paper they discussed possible mechanisms to explain these findings.

They did not include the Coronary Drug Study as it was not a primary prevention trial but they referred to it, to the niacin sub-group, as follows: "... the Coronary Drug Project reported 30% more deaths from accidents, suicides and homicides in men receiving niacin than in those receiving placebo." In fact, Canner et al (1986) to whom they attributed this statement, did not draw this conclusion. On the contrary, Canner et al did not find the slight increase in deaths in the niacin group over placebo to be statistically significant. Here is what Canner et al actually reported in Table A2.

	Niacin N = 1119	Placebo N = 2789
Non-medical causes of death	12	24
Percent (my calculation)	1.07	0.86

If the two groups were identical one would expect there would have been 10 deaths from the niacin group. An increase in 2 deaths in large groups surely is statistically insignificant, for it would take a miracle to have had both groups identical. Yet Muldoon et al (1990) dignify an insignificant minor variation in deaths by calling it a 30% increase in deaths. Canner et al did not even discuss the minor increase, as they would have if the difference had been statistically significant. The Coronary Drug Project does not support the claim that lowering cholesterol levels increases non-medical deaths. Nor was there an increase with Clofibrate.

However, there is evidence that lowering cholesterol by other means may have a significant effect in increasing non-medical deaths. McLoughlin and Clarke (1989) and Horrobin (1989, 1990) drew attention to the increase in non-medical deaths in cholesterol-lowering trials.

Following Muldoon et al's report there were a number of commentators. Law, Wald and Frost (1990), following an analysis of 16 therapeutic trials, found the increase in death of borderline significance. Smith et al (1990) reported there was no correlation between non-medical deaths and cholesterol levels in a study on 17,718 men ages 40-64 between 1967-69, analyzed in 1987. Ninety died from non-medical causes. The death rate was unchanged from the lowest cholesterol group (<4.11) to the highest (>6.05). Nor was there a significant correlation between hostility and cholesterol levels ($r = 0.016$) in 4246 men and 1742 women. Smith et al suggested one should look not at cholesterol but at the methods for lowering cholesterol as a possible cause. Shaper and Cook (1990) found no evidence communities with lower cholesterol levels had a higher incidence

1. 3A - 2727 Quadra Street, Victoria, B.C. V8T 4E5.

of non-medical deaths, and suggested that in studies of these deaths one should take alcohol into account. I believe this is a valuable suggestion since alcoholics are not known for the quality of their diet, are apt to be on a low fat diet because of their consumption of alcohol, and do have a higher death rate from non-medical causes. The percentage of men and women over 6.5 (252 mg) is 44.5% for both districts and for over 8 (310 mg) is 10.5%. It seems to me these are rather tiny changes, even if

statistically significant. Very minor differences which are random do show up as significant in statistical analyses.

Finally, Narayan reported some data which he thought did show a relation between cholesterol levels and non-medical deaths. In the Grampian region of Scotland, in Banff and Buchan, cholesterol was lower and deaths higher compared to Aberdeen. He presented the following Table.

	Banff and Buchan		Aberdeen	
	Men	Women	Men	Women
Mean serum cholesterol	6.3	6.4	6.4	6.5
% with cholesterol over 6.5	41	48	43	46
% with cholesterol over 8.0	10	11	12	9
Death Rate	79		63	

Assuming men and women were equally represented, then the difference is only 4 mg percent (246 and 250).

To summarize, it appears likely that:

1. There is no real causal association between cholesterol levels and nonmedical deaths.
2. There may be a relationship between methods used to lower cholesterol and non-medical deaths.
3. There is no evidence that niacin, a vitamin not a drug, which lowers cholesterol effectively, increases non-medical deaths.

All these statements point to only two major factors: (1) special low cholesterol diets, (2) the effect of cholesterol-lowering drugs not related to their hypocholesterolemic activity, i.e. to a direct action of these treatments.

I think it highly unlikely low cholesterol diets alone are responsible, unless the subjects of these studies on low-fat diets maintained their caloric intake by increasing sugar consumption. I think there is powerful evidence the drugs had some unexpected effect. A search must be made to test these ideas.

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