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TWIN CITIES

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March 21, 1981

Harriet S. Meyer, M.D., Senior Editor  
Journal of the American Medical Association  
535 North Dearborn  
Chicago, IL 60610

Dear Doctor Meyer:

A copy of the review in JAMA February 6, 1981, p. 511, of "Seven Countries--A Multivariate Analysis of Death and Coronary Heart Disease," has just reached me here in Italy. Dr. Feinlieb comments on the absence in the chapter on the diet of a presentation of the relationship of total mortality to the diet and infers "that there is a negative association, although perhaps not significant, between total mortality and percent of dietary calories from fats."

I regret that I did not specifically present the data on this point; it was a problem to keep the numbers of tables and figures in the book within practicable bounds. However, in the book the total death rates are given for each cohort in Tables 4.1 and 4.2 and the relevant dietary data for each cohort can be read, with some effort I admit from Figure 14.2 (% diet calories from total fats), and Figure 14.3 (% diet calories from saturated fats).

In ten years 1,507 men died, the cohort rates per 10,000, standardized by single years of age, ranging from 656 for Crete to 1,652 for Slavonia. Those all-causes death rates are to be compared with the dietary characteristics of the cohorts estimated at the start of the follow-up. There is no significant relationship between death rate and the mean percentage of calories from total fats in the diet, the coefficient being  $r = -0.0$ . In contrast, the coefficient correlation between death rate,  $y$ , and mean percentage of calories from saturated fats,  $x$ , is  $r = 0.47$ , the least-squares regression being  $y = 835.28.7x$  with a standard error of the slope of 14.4.

Ignoring direction, the observed relationship would occur by chance in about 5% of trials. But here the prior hypothesis was that mortality would increase with increasing saturated fat in the diet and the chance of sustaining that hypothesis as observed would occur by chance in less than 3% of trials.

However, I join with Dr. Feinlieb: In "ecological correlations....it is difficult to rule out the effects of numerous other factors which differ in the respective groups." As in almost all such epidemiological studies cause and effect is not proved. The most that can be concluded is that the results are consistent with the hypothesis that the all-causes death rate of middle-aged men in such populations increases with the proportion of calories from saturated fats in the diet of the population. Obviously,

Harriet S. Meyer

-2-

March 21, 1981

the rule would not apply to populations with large numbers of deaths from malnutrition and infectious diseases. Among the men in the Seven Countries Study evident malnutrition was extremely rare and among 1,507 deaths only 71 could be attributed to infectious diseases, 62 of these deaths being caused by tuberculosis.

Sincerely,



Ancel Keys, Professor Emeritus

P.S. This letter is written from my Italian address: "Minnelea," 84060 Pioppi (SA) but will be mailed from Minneapolis (410 Groveland Avenue, Minneapolis, MN 55403) where I shall be from April 2 until May 9. From May 12 until mid-July I shall again be at Minnelea.

A.K.