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To H.B. from A.K. 3 May 1981

Thanks for the extensive "running commentary," a welcome change from the general rule of no response or not until too late to be useful from colleagues to whom I give ms. for comment.

I have incorporated some of the suggestions in a re-do. The most important alterations are the summary and title page, copies enclosed. (& p.8).

Re cause-and-effect I cannot join epidemiologists who wish to escape the limitations of epidemiological evidence by talking about "consistency" and "congruence." If such tests are met the inference is much strengthened but inference is not proof.

Enough of such matters. The most important part of the re-do is the result of doing what I should have done before, namely applying partial correlation to BP, cholesterol and diet. You'll see the result on p.8.

Most of my 12-hour days here are given over to re-doing the ms on 30-year mortality of the CVD men. NEJ Med. says it is too long and partly published before. If you want to see the new product and consider being an "author" let me knwo.

H. Blackburn (May 1, 1981)

Running Commentary on article on Diet and Death Rate by Ancel Keys

Thanks for seeing this early. I have little substantive to suggest.

I wonder if you might not want to consider adding a sentence in the summary after the sentence now ending on line nine, ". . . r=.84 for coronary deaths," that "the correlation for all causes of death was largely explained by the correlation with coronary death," (if this is indeed so)? Your low key sentence, long afterwards toward the end of the summary, i.e. "The death rate from causes other than coronary was not significantly related to the diet," is sort of lost in the more dramatic impact earlier of "the negative correlation of all causes mortality with monoenes and polyunsaturates." Your statements are quite accurate. It is a question of possible perceptions and emphasis.

Might it also make things a little clearer if in every case you would describe differences as <u>population</u> differences so that the reader can more readily and consistently understand you are dealing with differences between populations?

I know you are saving cancer for another publication, I suspect it might, however, strengthen the relevant sentence below to add that: "the death rate from causes other than coronary (<u>including all cancer</u>) was not significantly related to the diet." You might want to qualify that and add the reference to your other papers. In other words, does your concluding sentence really entirely "negate the idea" about diet and mortality when there is absence of specific mention of cancer? Again, your generic statement is quite true that the advantage will not be "offset by more deaths from other causes." But it does not entirely satisfy the reader in regard to <u>specific</u> other causes.

I think it might be helpful to have a subtitle after the first paragraph on page four indicating that we are now dealing with Results. The dietary measures appropriately remain under Methods.

This is the first time I've seen you use fatty acid ratios in describing

the diet. Do you think it might be useful to give an explanatory sentence as to why you used the saturated-unsaturated ratio as well as the P/S ratio, since the former is not a commonly used variable?

In the discussion on the diet-blood pressure relationship, as you once did so neatly with the saturated fat-sugar correlation, it might be an added and useful speculation (in the absence of reliable data?) that a correlation between saturated fat-salt intake may be operating here.

The Belgium and U.S. Railroad sections are very neat.

You might emphasize the correlations between individual diet and death rates within cohorts by adding these words and emphases in paragraph one on page nine.

I often think of the fruitful discussions in the international seminar at Pioppi (and elsewhere) on the weakness of the terms "proof and cause." You often make the negative (though correct) point that descriptive epidemiology doesn't provide "proof." Are not the rules and criteria now well laid out for the inference of cause from statistical associations, including the crucial point of congruence? I personally find their use as accurate and more positive. Rather than saying "epidemiological studies can never prove cause," (however true that may be within your context), why not indicate simply how well or poorly observations fit the established criteria for causal inference (strength, consistency, dose effect, congruence, prediction, etc.), that is, the important test!

I remain sensitive to vague impersonal criticisms, and theoretical types of scapegoats such as "enthusiasts," or "fanatics." I feel these labels identify no one and accomplish little unless one is specific about the "evil" target.

Admonitions about unidentified people labelled enthusiasts or skeptics might be replaced by some such as this, starting in sentence two, page nine: "Causal inference from epidemiological studies, even prospective ones such as the Seven Countries Study, can only be seriously considered when a series of well established criteria are met (give reference). However, consistency or inconsistency of the findings in respect to the hypothesis of interest is what can be said with confidence."

Later your "skeptics and critics" are also vague as targets. Why not? "But the same limitation applies to rejection of a hypothesis; negative conclusions should be considered by the same rules of consistency and congruence."

In your very last sentence, you omit to provide the interesting data from the book showing that the cohort CHD death rates are highly correlated with nationally reported death rates. I believe to have such a last sentence, even with regard to the Seven Countries Study, requires to cite that evidence. The further extrapolation from 12,000 men in the cohorts to national experience in Canada-Australia-New Zealand will certainly be criticized and may not be necessary to your point.

Finally, on the tables I know you have a common pattern that you like to use. Readers appreciate, I suspect, a clear title and heading on tables to orient their thinking, with the details in a legend, e.g. The Seven Countries Study: Diet and 10-Year Death Rates. Not Important.

Thanks. First rate.