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Dr. Ancel Keys 410 Groveland, Apt. 802 Minneapolis, MN 55402

Dear Ancel:

I enjoyed reading your CVD manuscript on body fat. It seems to me you've considered and answered most of the questions that should be raised. The manuscript is extremely straightforward, crisp and to the point.

I'm interested that you've changed CVD or Business and Professional Men's Study to Twin Cities Prospective Study. Fine. It might be well to refer to it as "formerly known as" so that old friends can recognize it and the literature can make a connection. Not very important. I like the new name.

The most obvious question that is not addressed I believe, is that of the effect of individual change in weight. I could understand how this would vastly complicate your analysis and you might want to avoid it or approach it separately. However, change in weight in the early or middle part of the observation period, would be more interesting of course than late change, which we did not measure.

Other than that, my remarks are minor and editorial. You might want to use "body fatness and weight" instead of just the term fatness throughout. I was a little confused by the term "relative fatness" when I believe most of the values are not relative, say to a population standard. Weight relative to height, or girth relative to something else is fine, but the term relative fatness confused me a bit.

Despite your touching on it in several places and considering blood pressure in the multivariate analysis, the sequence of fatness or elevated relative weight leading to elevated blood pressure and <u>leading to</u> early death could be examined, it seems to me in your customary straightforward way rather than by multiple logistic analysis. At least we need to know how much blood pressure accounted for the excess of nonsurvivors among the fat. I agree that this issue is not important if there is no relationship of fatness to survival. However, you <u>did</u> find a relationship and if disappearance of significance was due primarily to blood pressure, we still don't get away from the pathogenic chain from obesity.

A small point is your strong statement that "the majority of smokers have quit many years before death" was not documented. You did not describe for the naive why you used the log linear analysis.

Age at entry was very interesting and I think would deserve a small table as well.

Note that in the introduction and methods you don't mention the total number of subjects, which should appear probably in your second sentence "Among X men, aged 45-55 at entry, 172 were dead, etc."

One of the most helpful things to do when results are disparate is to try to analyze the reason for the disparities. Since Framingham's results were unique, it might be useful to comment on possible reasons for their uniqueness. I've always been bothered by the "subterfuge" in the "30-year followup" which is in no sense a 30-year followup, rather it's a 2-year followup repeated 15 times. In most of their studies there is no consideration of the original cohort. Since Framingham makes the most noise in the field, and most noise about this particular issue, it might be useful for you to get their latest paper and dissect it a bit.

Thanks for letting me see this

Otherwise, I hope that our data center has been responsive to your needs for getting data on the VAX and I appreciate your continuing to look for support for this. With the remarkable quality and consistency of the work you produce there's no reason on earth why you shouldn't get support from any size NIH grant you want. If we can help you with the frustrating details of rewriting your grants, I think that's a better approach than being upset that they turn us down. This is routine nowadays that study sections "need educating" and it takes at least two and sometimes three proposals to educate them and to write things in a way that they can grasp. The pink sheets you gave me on the last one suggested that you may not have been responsive to an earlier pink sheet suggestion. Since I didn't have the earlier pink sheets I don't know what your application was not responsive to, so I can't be helpful. But we have been pretty effective with grants in recent years if you would like us to give it a going-over, provide us with the information.

Thanks for the early reprint. I am putting together a group of "seminal reports" of the Division before 1972 for the education of the faculty and students who are not aware of past history. In that regard it might be nice if we could again put you on for a spring or summer division seminar so that at least each class in the School and Division can get exposed to you once a year. Would you be willing to do this?

Cordially,

Henry Blackburn, M.D.

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