of the sample, increase the statistical validity. The weakness of this is the known remarkable variation between one observer and another. We in our own group, and there are three of us engaged in rheumatology in our group—have tested this repeatedly; and although we have tried on many occasions to standardize our observations and have seen patients jointly and in conference, we still find a distressing degree of variation between the three of us who work so closely and harmoniously as a unit. To have 11 different observers from 11 widely scattered clinics making observations which are then stated to be of an identical character seems hazardous at least. There were a number of exclusions in the ARA–CCC study which would certainly weaken the trial's validity.

For example, the patients were to be "out-patients or domiciliary hospital patients," but it does not say how much of each sample comprised the total. Certainly a rheumatoid arthritic in a domiciliary hospital environment is much more likely to have a quiescent disease than one in an outpatient environment. The exclusion of all patients who have had antirheumatic therapy would effectively eliminate all cases of even moderate severity. So you would have to assume that most of the cases in that study were cases of mild degree.

Senator NELSON. I have a question in reference to your sentence that a rheumatoid arthritic in a domiciliary hospital environment is much more likely to have a quiescent disease than one in an outpatient environment. In setting up a double-blind test, or any kind of study, if those making the study were comparing the person in a domiciliary facility versus one who is outside of it, it would be a fault in the study immediately, would it not?

Dr. ROTHERMICH. Oh, yes.

Senator NELSON. In other words, do you not, in setting up studies, compare age groups and try to get them as comparable as possible?

Dr. ROTHERMICH. Yes, and this factor, Senator Nelson, of putting an arthritic at rest, not necessarily bed rest, but outside of an environment that is distressing to him, putting him away in a domiciliary hospital environment, you see, is much more likely to allow his disease to become quiescent. So they should have said "we have x number of patients who are hospital domiciliary type and we have x number of patients who are outpatients," and given the result of those studies in the given categories.

Senator NELSON. In other words, you would compare domiciliary patients versus other domiciliary patients and the outpatients versus other outpatients?

Dr. ROTHERMICH. Yes. I would like to add the point, too, that this study was being done by 11 different centers, and they have, I think, 110 total patients. I think half or more of the centers had less than 10 patients in their study group, and some of them as few as four patients. Now, Dr. O'Brien made the statement before this committee at another point that some of the reports in the literature were only of 10 patients or so and any work on such a small number—I cannot think of his exact words, but the substance of it was that it was meaningless, or had no validity.

Now, he was referring to other types of work. But I would point out to you, Senator Nelson, that the components of this combined study, you see, had less than 10 patients in many of their centers.