In nutritional studies, all of the enrolled subjects are typically started on experimental and control treatments on exactly the same day. The ample supply of healthy subjects willing to participate in a nutritional study enables this kind of study design. Moreover, the requirement for keeping nutritional studies subjects confined in a "metabolic unit" during the course of the study, to prevent subjects from consuming non-study foods, necessitates that all subjects begin the trial on the same date (34).

It is also the case that some clinical trials are concluded before the event of interest has occurred in every single one of the subjects. This situation can lead to bias, where the physiological properties of patients enrolled early in the trial differ from those enrolled late in the trial. As articulated by Bland and Altman (35) "we assume that the survival probabilities are the same for subjects recruited early and late in the study. In a long term observational study of patients with cancer, for example, the case mix may change over the period of recruitment."

V. SAMPLE VERSUS POPULATION

The terms *sample* and *population* are standard terms in statistics. The term *sample* refers to data acquired by actual measurements. The investigator has the option of testing one sample, taken from a population, or of testing more than one sample, taken from the population. In discussions of statistics, it is the case that the term *sample* refers to a group of objects, for example 50 drug tablets, while the term *population* refers to the entire batch of 10,000 drug tablets that was manufactured. In statistics, it is the case that the term *sample* refers to 100 subjects enrolled in a clinical trial, while the term *population* refers to the entire world's population of people with the disease of interest. The sample needs to be representative of the population.

The term *population* can refer to a hypothesized, underlying value or to an imaginary, idealized value. In some situations, it is possible for the researcher to measure a parameter of interest from all members of the population. But often, it is impractical or impossible to measure the parameter in all members of the population. Data acquired by analyzing a sample are subject to variations in the properties of the sample and to variations in the techniques used by the investigator. For example, in a study of 50 human subjects, 15 of the subjects may have a mutation in a growth factor receptor gene, while the other 35 subjects have the wild-type gene. Or, in a study of 50 human subjects, 5 of the subjects may have forgotten to take two of their drug doses, while 45 of the subjects had remembered to take all of the drug doses. But data acquired by analyzing a population take into account these and all other variations, and data acquired by

[34] Margen S, Chu JY, Kaufmann NA, Calloway DH. Studies in calcium metabolism. I. The calciuretic effect of dietary protein. *Am J Clin Nutr.* 1974;27:584–589.

[35] Bland JM, Altman DG. Survival probabilities (the Kaplan-Meier method). *Brit Med J.* 1998;317:1572.