pected change of zero was derived from a chronic schizophrenic sample and was not felt to be representative of the newly admitted patients.

Armitage[1] has discussed two models applicable to patient pairs. In the case where there is an "all or none" therapeutic outcome, e.g., death or infection, each pair of patients is classified as $++$, $+-$, $-+$, or $--$. The $++$ and $--$ pairs are disregarded, and the remaining pairs plotted in the order of their evaluation. To calculate his decision lines, it is necessary to specify two alternative hypotheses and their associated coefficients of risk. Armitage bases his alternative hypotheses on the known success rate of the control treatment and his judgment of what would constitute a meaningful increment of successes for a new treatment. One not-so-apparent disadvantage of this method is that the number of discarded pairs can be quite large, e.g., in his sample problem, a decision was reached after 14 pairs had been evaluated but 31 additional pairs were tied and therefore disregarded.

In the case where there is a quantitative measure of the success of treatment available for each member of the pair, Armitage recommends the sequential t test. The expected mean difference under the null hypothesis would be zero, and the alternative hypothesis can be set by the experimenter so as to represent a clinically important difference. This latter value can be determined from normative data obtained in previous investigations if they are available.

A variation of these two methods has been presented by Sainsbury and Lucas,[10] who used each patient as his own control in an evaluation of prochlorperazine in outpatients suffering from acute anxiety. The patients in their trial received either prochlorperazine for one week followed by placebo for a week, or the reverse order, determined at random. The outcomes were plotted as suggested by Armitage.

Finally, it is worth noting that, in all of these models, the experimenter must decide what constitutes a clinically important difference and what degree of risk he is willing to tolerate in reaching his decisions. Although the latter should not be determined without careful thought, convention leads us to set these at 0.05 or 0.01. Defining the difference that is considered to be important enough to detect is more difficult. It is possible in some instances to base this definition upon previously collected data or, as Armitage suggests, to select a value that, if present, has a reasonable chance of being detected with the cases available for evaluation. As he points out,[1] "Eventually a compromise will be reached between the requirements of sensitivity in detecting small differences (which tend to increase the length of the trial) and those of economy (which tend to decrease the length)."

SUMMARY

An application of sequential analysis in a clinical trial of phenothiazine derivatives is described. The results were found to be reasonably consistent with those obtained from a more conventional statistical approach. Advantages and disadvantages of the method as well as alternative models are discussed.

RESUMEN

Se describe en este trabajo una aplicación del análisis secuencial en una prueba clínica