THE ANALYSIS AND PRESENTATION OF RESULTS

J. Knowelden

The distinguishing characteristic of a controlled clinical trial is the quality of the planning which is done before any observations are made. The impact of a well-planned trial will depend to a great extent, however, on the quality of the report which is published; readers must be convinced that the work was worth doing, was well done, and that the findings are relevant to the clinical situations they might have to face. To this end the report should aim to present the final conclusions backed by the fullest evidence.

The introduction to the report should state clearly the question that the trial is intended to answer. This may require some review of the literature, which, however, need not be extensive unless it is necessary to show why previous reports are unacceptable, or what differences of opinion currently held are to be resolved by the present trial. This section must, however, discuss the choice of drug and the kind of illness which is to be treated.

As the controlled clinical trial stands or falls on its plan, the report must describe this in detail. It is important to give the diagnostic criteria employed, so that it is evident that the patients selected were homogeneous in respect of their illnesses, and so that it is obvious in what clinical conditions the results of the trial might later be applied. The recruitment of patients, whether for example from all admissions to the wards or out-patients which satisfy the diagnostic criteria, or from some special source, and the method of allocation to Treated and Control groups, require special attention on the report as this is the crucial stage in a trial. The therapeutic régime to be given to both groups must be stated, in particular whether the dose is to be fixed or left to the physician's discretion, together with the reasons for this decision. The results of many well-conducted trials have been criticized on the grounds that the dosage employed was inadequate or ill-adjusted to individual patients' requirements. The plan also includes the choice of clinical and laboratory tests used...
to measure the patient's progress, their timing and the scales by which they are to be interpreted, and the arrangements made to ensure equality of observation, both objective and subjective, on the Treated and Control groups. The section of the report dealing with the Plan should also include mention of any ethical problems in the organization and conduct of the trial, and in particular the grounds on which it was agreed that patients could be withdrawn.

The analysis proper should begin with a statement of the number of patients who entered the trial and who satisfied the diagnostic criteria. An account should then be given of those patients who withdrew from the trial at different stages and the reasons for their withdrawal. Sometimes the withdrawal may be coincidental and unrelated to the treatments being given; the diagnosis may be revised and found to fall outside the category specified for the trial, an intercurrent infection or distinct additional illness may occur, or the patient may be unco-operative or be moved elsewhere. With this type of exclusion it is usually sufficient to show in the report that it occurred with equal frequency in Treated and Control groups and cannot have disturbed the group comparisons.

A more difficult problem arises with exclusions which may be related to the treatments given, e.g. a patient who is found to be sensitive to penicillin, who develops salicylism on the agreed dosage of aspirin, or haemorrhagic complications when given anticoagulants. There will always be a group of patients who exhibit side-effects, and while with some it may be possible to continue treatment, with others it may be necessary to stop. Exclusions of this kind often operate unequally in Treated and Control groups, so that those who continue the full course are not necessarily alike as were those originally allocated. Here there are two alternatives:

(1) The exclusions can be counted as failures to the selected treatment, and the further analysis made on a comparison between the remainder who completed Treated and Control régimes;

(2) the groups, as originally allocated, can be compared in their progress, although some members failed to keep to the treatment, making here a comparison between those intended for Treated and those intended for Control régimes.

One or other or both methods of analysis may be presented, the
choice depending on whether it is important to emphasize the disadvantages of a particular therapy.

The intention in a controlled trial is to provide groups of patients, alike as far as possible, except that they receive different treatments. Before the progress of the groups can legitimately be compared it is important to see that they were initially alike. The analysis must therefore include a section on comparability of the groups. On general grounds this should usually show equality in age- and sex-distribution. The frequency of presenting symptoms, duration of illness at the start of treatment, number of previous attacks, and severity, are characteristics which can often come into such comparisons. In addition it is often useful to include some personal characteristics such as occupation or income, or the history of other illnesses unrelated to the one under treatment, as these independent factors can be a valuable indicator of the likeness of Treated and Control groups.

The analysis of progress of patients in a controlled trial may take various forms. In the simplest forms, as in the early trials in tuberculous meningitis, it was a measure of the frequency of survival or death, or, as in pulmonary tuberculosis, the proportion recovering as judged clinically, radiologically and bacteriologically. Where recovery was the rule before the introduction of a new treatment under trial, as in pneumonia, the progress may be measured in terms of speed of recovery. A time scale is useful in another sense in measuring the proportion of cancer patients surviving a period, often five years. In a chronic disease in which complete recovery is not expected, e.g. in rheumatoid arthritis or bronchiectasis, the measure of progress may be the degree of rehabilitation assessed both subjectively and objectively. Each trial will have its own most appropriate measures, and the analysis will vary accordingly.

Despite this variation, certain general principles can be suggested. It is rarely necessary to list individual patients and their behaviour in this report, and such lists are more often confusing than helpful. Nevertheless the results of the trial should be fully tabulated. As the basic comparison is between the different treated groups, the tabulations should give the evidence on each clinical and laboratory test, using frequency distributions where possible, or summaries of these by proportions or means. It is helpful to the reader if the format of the tables is approximately the same throughout. Some of the findings may be given for the total Treated and total Control groups.
and this may be sufficient. More often the total groups are themselves heterogeneous, and the analysis should make comparisons between smaller subdivisions of the totals. In the common cold trial it was important to see whether antihistamines failed in early as well as in late cases, in those with allergic histories as well as in those without. The conviction with which the results of a controlled trial can be presented may depend on the ability to show that the consistency in the response of the different sub-groups is compatible with the various clinical pictures thus differentiated.

The purpose of the text of the report is to guide the reader through the tables, emphasizing the principal findings. It does not have to include every figure shown in the analysis, but at least for the early tables it should explain the method of analysing the data. It should quote the main entries on which comparisons are based, and comment on the statistical significance and practical importance of any difference observed. Diagrams may be invaluable to illustrate main points, but should not be used as a principal method of presenting the analysis. As a rule they are most effective when they do not attempt to show more than one factor at a time. By contrast a single table can readily show the influence of several factors, and is a far more efficient way of presenting results.

When all the data have been presented the next stage is to discuss the various indices used in the study to arrive at some final conclusion. If all measurements, subjective and objective, clinical and laboratory, are consistent in the picture they give of the relative merits of the Treated and Control régimes, this section can be simple and brief. There may, however, be conflict; the subjective benefit of one treatment may be out of proportion to that measured objectively, and clinical improvement may not run parallel to changes in laboratory tests, or the advantage of one therapy may be associated with serious side effects. In these situations the discussion may become a very important part of the paper and will be much more extensive.

It is traditional to provide a summary at the end of the report. Very often this will be read first, and only if it is informative will the reader look at the whole paper. It is worth while taking considerable trouble to see that this summary gives the main features of all phases of the trial, and that it quotes selected numerical details to illustrate the argument.

The analysis of the results of a trial and the presentation in a report are an important task. Although many individuals will have taken
part in the whole enterprise and will be responsible for the joint
conclusions, there is much to be said for making one person the
chief author. Although he cannot please all his collaborators, a
single author is more likely to produce a coherent document than
would a group, and is best placed to ensure that text and tables are
consistent throughout in the story they tell.