groups (e.g., age, gender, risk factors, degree of disability, etc.). Small samples (less than 30 subjects) do not typically lead to the benefits of randomization. 2) The sample is homogenous.[4] A homogenous sample is achieved with the use of strict subject screening criteria. This is effective if there is clarity of the clinical question so that the target population can be clearly defined. 3) All subjects remain in the study until completion.[5] Differential attrition between treatment and control groups leads to significant bias of results. 4) The treatment and control conditions are concurrent.[6] The random procedure should not allow for long periods of time where there is assignment to one group versus another. Many historical intervening factors can influence the experiences of the cohorts as they progress throught the study, and thus may influence why subjects elect to "drop out."

Internal validity will be strengthened if the constancy of the experimental and control conditions is assured. It is often recommended that all persons except those remotely involved in the study monitoring be blinded to the subjects' group assignments.[6] This is to assure that experimenter bias is not introduced into the protocol application due to expectation of study results. The length of the protocol for any individual subject, as well as the length of the entire study, should be as short as possible to reduce the opporltunities for extraneous factors interfering with protocol implementation (e.g., the vagaries of history, deterioration or changes in staff's application of the protocol, variations in the technical performance of equipment over time). The technical skill of staff needs close assessment, training, and retraining as necessary to maintain performance at a standard level. The technical performance of equipment needs careful assessment before the study and throughout its duration. Equally important is attention to the control condition.[5] Preventing contamination of the control condition with elements of the treatment is important to reduce dilution of treatment effect and minimize resentful demoralization of subjects not getting the experimental treatment.[7]

Quality assurance procedures that frequently monitor the study protocol are critical to internal validity. This becomes even more important in lengthy trials.

An example of procedures used to assure study integrity follows. In a clinical trial by Potempa et al.,[8] post stroke subjects were randomly assigned to an experimental aerobic exercise treatment group or to an "attention" control group consisting of head-to-toe passive range of motion. In order to maintain protocol integrity, investigators, including statistical analysts and laboratory staff who performed outcome measurements, were blinded to the subjects' treatment condition. Only the staff performing the treatment and control protocols were aware of subjects' group assegnments. The laboratory where treatment and control conditions occurred were similar by design but physically separated to reduce subject acquaintance, in that subjects came for treatments three times per week and were likely to meet each other if the locations were in proximity. The quality assurance measures included staff training and periodic retraining to standard, designated equipment checks for standard performance and equilibration, and inter-rater reliability assessment of all observer-rated outcome measures. After baseline reliability was established, test re-test reliability assessment was performed on a random 10% of all exercise tests.

The Need for Pilot Work

Prior to the construct and submission of a grant proposal for a clinical trial, it is generally necessary to conduct pilot studies, and may be a requirement of larger funding agencies. Pilot studies serve several purposes. A pilot study may be designed as a small-scale version of the planned clinical trial, which is aimed at testing the planned methods and measures. Therefore, such pilot studies assess the feasibility of the planned clinical trial, determine the adequacy of the instrumentation, and identify problems with data collection strategies and other methodological issues. Pilot work may also consist of a subset of a planned clinical trial, designed to answer a methodological question prior to the development of the full research plan.[9] For example, the measurement of maximal oxygen consumption (VO2max) is reproducible in healthy adults, although this had not been demonstrated in stroke patients. A pilot study was conducted to document the reproducibility of VO2max in stroke patients