Guest Editorial

In the hierarchy level of evidence, randomized controlled trials (RCT)´s are considered the highest level for evaluating new therapies. They offer high quality evidence for clinical practice, approval of new drugs and treatment methods, and decision-making of public health policies. When a proven treatment is available, and a new treatment is to be evaluated, a RCT is designed to evaluate the superiority, equivalence, or non-inferiority of the new treatment relative to the established effective treatment. In RCT's patients are randomly allocated to two or more groups: the experimental group (treated), the control group (no treatment), conventional treatment, or a placebo.

A placebo is used in RCT's to mask whether a treatment is given or not and consequently to control for the psychosomatic effects of the offering treatment. Ethical concerns debate that if a proven effective therapy or standard treatment is available; a placebo is not justified even if they are used to evaluate new treatment conditions. Placebo-controlled (PC) advocates voice that placebo trials are necessary to determine the efficacy and safety of many treatments. If a RCT did not include a placebo, it may be unattainable to depict a drug's potential for harm. Defenders of placebo controls in RCT's argue that their use is valid and ethically justifiable when sound methodological considerations are taken and participants are not exposed to unnecessary risks of harm that compromise their well-being.

PC trials must meet ethical standards if they are conducted. All staff must understand the procedures and requirements needed to protect the participants of the study. The clinical trial protocol should be carefully evaluated and approved by an Institutional Review Board to safeguard the overall health of the participants and protect their rights. Another essential requirement of a PC trial is a voluntary informed consent to ensure that participants understand the nature of the study, its potential risks and benefits, and that they can withdraw without penalty from the study at any time. Patients willing to participate in clinical trials may make rational and personal decisions regarding their participation or non-participation in the studies. They should have all the information regarding equipoise and the plausible outcome of each treatment group.

The dilemma confronting clinician/investigator exists and it's challenging to make a balance. The role of clinicians is to care for their patients, while the role of an investigator is to care about their research. This dual commitment conflicts whenever a clinical investigator comes face to face with a patient/study participant. Therefore, it is important that the clinician /investigator wears at all times a different hat. Wearing different hats involve acting in the best interests of each patient while considering the implications of not following intent-to-treat criteria and adhere to ethical protocols. A proposed solution in the clinician/investigator conflict is to carry out adaptive randomization trials. Adaptive randomization involves assigning therapy to the treatment group that has the best outcome during the trial. Adaptive randomization aims to decrease the number of patients allocated to the least-successful treatment. It must be used in RCT's that seek only one outcome of interest and the results must be detectable in a short period of time. One disadvantage of this type of randomization design is that more patients are needed, thus prolonging the investigation.

Randomization in RCT's will always represent a challenge for researchers. Randomized consent reduces the psychological burdens of the investigators, but in some instances it is considered ethically unacceptable. Additionally, the difficulty in designing a trial involving a community control group in RCT's is a matter of concern. RCT's in some instances may represent a double-edge sword and should be considered: when the therapy being tested is potentially life-saving, to keep pace with evolving technologies, when RCT's are not the best approach for research hypotheses, and when non-randomized data provides compelling evidence.

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