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Symposium on Equipoise and the Ethics of Clinical Trials

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Symposium on Equipoise and the Ethics of Clinical Trials

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Randomized controlled trials (RCTs) are generally considered to be the best method of evaluating the effectiveness of medical treatments. As in all research involving human subjects, RCTs pose an inherent tension between pursuing socially valuable knowledge and protecting research participants. In addition, they face the ethical challenge known as “the RCT dilemma”: How is it possible for physicians to offer optimal, or competent, medical care to patients in need of treatment while conducting scientific experiments that select treatments randomly? The leading, widely endorsed, answer to this question is the doctrine of “clinical equipoise,” developed in 1987 by Benjamin Freedman. According to this doctrine, RCTs are ethical when there is a state of uncertainty in the medical community regarding the therapeutic merit of the investigational treatment and control interventions being evaluated, such that no patient is randomized to a treatment known to be inferior to the established standard of medical care.

This issue of *The Journal of Medicine and Philosophy* is devoted to a debate about various forms of the doctrine of equipoise. At stake are basic theoretical and practical issues concerning the ethics of RCTs. Are the ethical principles governing clinical trials essentially similar or fundamentally different from those governing medical care? Under what conditions are placebo-controlled trials ethically acceptable? When should RCTs be stopped earlier than planned in view of emerging data regarding the efficacy or harm of interventions under investigation?

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In the first contribution to the symposium, Benjamin Djulbegovic examines the central concept of uncertainty that underlies equipoise. He clarifies various types of uncertainty relating to the therapeutic merits of treatments and the implications for trial design aimed at answering clinically relevant questions.

In the second essay, Alex London criticizes both the proponents and opponents of equipoise for failing to provide an ethically satisfactory standard for determining the level of acceptable risks to subjects of clinical trials. Distinguishing between the personal and basic interests of individuals, he develops operational criteria for allowable research risk.

Paul Miller and Charles Weijer undertake a wide-ranging critique of the work of Franklin Miller and colleagues, which has rejected clinical equipoise and offered an alternative ethical framework oriented to avoiding the exploitation of research subjects.

Fred Gifford argues that the clinical equipoise is unclear and ambiguous, making it unsuitable as an operational standard for the ethics of RCTs. In addition, he endeavors to demonstrate that clinical equipoise promotes premature stopping of RCTs before sufficient evidence is accumulated to guide reliable policy decisions regarding clinical practice.

Franklin Miller and Howard Brody contend that the doctrine of clinical equipoise is defective by virtue of conflating the scientific orientation of clinical trials with the therapeutic orientation of medical care and by providing incoherent guidance relating to risk-benefit assessment. They respond to criticisms of an alternative ethical framework based on protecting subjects from exploitation and suggest issues that deserve further consideration.

Finally, Robert Veatch suggests that equipoise, whether of scientists, clinicians, or subjects, is irrelevant to the moral justification of randomization. He argues that there are morally acceptable reasons to justify trials even when any of these players is not in equipoise. Since equipoise is an evaluative judgment that can be idiosyncratic, a potential subject can be in equipoise when scientists and clinicians are not and vice-versa and that, as long as a subject gives adequate consent to being in a trial, even the subject need not be in equipoise.

The thoughtful and thought-provoking contributions to this symposium on equipoise illustrate that there are fundamental disagreements about the ethics of clinical research. Whether (and how) the RCT dilemma can be resolved, or whether it should be set aside as ethically irrelevant, remain open questions. We hope that this exchange of views will help in stimulating the work that needs to be done to clarify the basic points in contention and develop reasonable ethical positions on the design and conduct of randomized controlled trials.