

Determining Research through Underdetermined Treatment

Paul Miller and Charles Weijer defend the concept of equipoise in medical research in a recent journal article.

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When a medical expert cannot responsibly favor one treatment over another—when the available evidence does not indicate (or underdetermines) what is the best treatment—the treatments are in equipoise. Certainly, this happens in clinical practice every day; however, equipoise is applied by medical practitioners, institutional review board members, and bioethicists most frequently in the context of medical research.

Equipoise was initially posited as a standard for determining worthwhile research by Charles Fried. His conception places the responsibility of reckoning equipoise solely in the hands of individual physicians, an opinion that was challenged by Benjamin Freedman [1]. Freedman's argument was not against the position of equipoise itself but rather based on the fact that Fried's conception of equipoise was so fragile that it could not be reliably achieved. An individual physician may think that one treatment is superior to another, but this opinion may or may not be accurate and has the potential to be unduly influenced by preliminary research results [2]. Consequently, Freedman argued for clinical equipoise, a modification of Fried's initial term, in which the community of physicians, as experts, determines when treatments are in equipoise. The determination of clinical equipoise depends on a larger number and wider array of experts, thus the conclusion should be more robust [2].

Besides differing opinions on how to define the term, the basic concept of equipoise has detractors, most notably Franklin Miller and Howard Brody [3,4]. In a challenge to the validity of equipoise, they argue that the responsibilities of physicians in research are diminished—as compared to their responsibilities in clinical care—due to the aims of medical research [4]. In clinical care, physicians attempt to care for a particular patient, but in research physicians attempt to illustrate the validity of a specific conclusion. Accordingly, Miller and Brody endorse a framework for patient-physician interactions which is constituted primarily by obtaining informed consent and avoiding exploitation [4].

In a recent publication, Paul Miller and Charles Weijer add a new dimension to this discussion in their attempt to "rehabilitate" equipoise by defending it from the critique of Miller and Brody while simultaneously re-casting it from Fried's initial description. They begin by minimizing Miller and Brody's critique, stating that "an ethics of clinical research that gives primary place to consent requirements nevertheless must acknowledge the role of fiduciary obligations and broader social standards in defining the boundaries of consent as moral and legal justification" [5]. Miller and Weijer go on to discuss in detail the contributions of Fried and Freedman and label their conceptions of equipoise FE (Fried's equipoise) and CE (clinical equipoise), respectively [5]. Indeed, this integration of apparently conflicting views of equipoise is perhaps the most significant contribution in their analysis. Rather than attempt to settle the question of individual expertise (FE) versus collective expertise (CE), Miller and Weijer couple them as complementary concepts. "FE provides a moral condition that satisfies the demands of the continuing fiduciary relationship between physician and patient. CE, on the other hand, addresses the overarching need of the state to

protect its citizens from harm, and provide clear guidance to IRBs as to when a RCT may ethically proceed" [5]. In short, uncertainty about the best treatment must pervade the clinical encounter and the medical literature.

There are two significant advantages to Miller and Weijer's "rehabilitated" equipoise. First, unlike CE, it caters to physician autonomy in a profession both dominated and characterized by decision-making. When an individual physician makes a judgment about treatment effectiveness for an individual patient, that judgment is generally respected. Second, unlike FE, rehabilitated equipoise allows for a collective determination of equipoise regardless of any particular physician's view. In at least some sense, we can responsibly claim treatments are in equipoise so long as the community of physicians is in equipoise. To describe this relationship hierarchically, CE (that is, the equipoise of the medical community) constrains legitimate individual equipoise (FE). Only when both the medical community and an individual physician are in equipoise can the physician legitimately be in equipoise about the best treatments.

However, there are two noteworthy pitfalls of this "rehabilitated" equipoise. First, it makes no direct mention of patient input. Should patients have any say in determining equipoise? Karlawish and Lantos, for example, argue that patients should play a greater role [6]. If the input of patients is not to be included in the determination of equipoise, it seems as though this should be accompanied by an explanation. It is, after all, the patients' as test subjects—and not the doctors'—bodies and lives which are most directly affected by medical research.

Furthermore, does the integration of FE and CE really avoid the fragile nature of FE? Freedman argued for CE because leaving the decision in the hands of individual physicians was both indeterminate and allowed for undue influence on the basis of poor judgment. Yet does the coupling of FE with CE adequately limit the effects of such decisions? If the medical community is in equipoise (CE) and the physician is expected to make a judgment that is relatively independent of the medical community's collective views (FE), the grounds for individual judgments will be the very grounds that made FE unreliable in the first place.

As with many questions of bioethics, there may be no perfect solution. The enduring uncertainty in medical decisionmaking combined with the persistent push for more clinical research ensure that the challenges of equipoise in determining ethically sound research will continue.

References

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