Clarifying the Ethics of Clinical Research: A Path toward Avoiding the Therapeutic Misconception

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only a modest cost to subjects. Thus, in the allergic rhinitis trial, placebo controls can be used because the risk-benefit ratio of no therapy is only slightly less favorable than the risk-benefit ratio of any available therapy, and the resulting knowledge may contribute to the welfare of those who suffer from allergies.

On this alternative view, therapeutic beneficence is maintained as the moral standard for determining whether participation in placebo-controlled trials may be offered to subjects. It cannot be dispensed with in any event, because it provides the standard against which placebo use must be assessed to determine that the increment of risk to subjects is not excessive. Once this determination is made, subjects may be invited to consider whether randomization is a matter of “approximate indifference” in the light of their own values and goals (Veatch 2002). However, given the vagaries of assuring adequately informed consent in the real world of clinical research, therapeutic beneficence should be maintained as an independent, threshold standard for determining whether placebo-controlled trials can be undertaken with proper regard for the welfare of subjects. On the other hand, therapeutic beneficence does not constitute an absolute priority. When placebo-controlled trials impose only a modest increment of risk compared to best available therapy, then subjects may be invited to participate if doing so is necessary to contribute to the welfare of patients as a group. Miller and Brody are right about this conclusion but wrong about the underlying rationale.

References

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Much could be said about the analysis—with which I largely agree—offered by Miller and Brody (2002) of the justification for the use of placebos in at least some studies where partially effective treatments already exist. Here, however, I focus on one salutary implication of their argument, derived from their observation that physicians running clinical trials do not have a therapeutic obligation to offer optimal treatment. They note that the previous Helsinki approach appeared to confuse the obligations of researchers with those of clinicians in opposing the use of placebos when they are likely to be inferior to existing care. In fact, this confusion between the ethics of research and of ordinary clinical care appears rampant in the world of clinical trials. When it arises among subjects, which it often does, it is known as the “therapeutic misconception,” a phenomenon that my colleagues and I described two decades ago (Appelbaum, Roth, and Lidz 1982; Appelbaum et al. 1987).

A therapeutic misconception occurs when a subject transfers to the research setting the presumption that obtains in ordinary clinical treatment: that the physician will always act only with the patient’s interests in mind. In the research study, in contrast, the physician’s actions—including the use of randomization, double-blind procedures, adherence to strict protocols, and administration of placebos—may be undertaken because they advance the scientific validity of the research study, rather than because they serve the subject. Such deviation from the principle of “personal care” (Fried 1974) cannot be justified in the absence of the subject’s knowing consent to forego the usual advantages of the treatment setting. Altruism is the most obvious justification for a decision of this sort, though subjects may correctly perceive some self-interest at stake as well—for example, free medication, more careful follow-up, the chance that research advances will be of direct help in the future. But this kind of knowing consent is often absent.

Since our description of the therapeutic misconcep-
tion, it has been much discussed, and there has been no lack of data suggesting that its prevalence is substantial. The Advisory Committee on Human Radiation Experiments (1995), for example, based on interviews with 1,882 former research subjects reported, “Patient-subjects frequently expressed the belief that an intervention would not even be offered if it did not carry some promise of benefit; many certainly assumed that the intervention would not be offered if it posed significant risks.” Our current research suggests that as many as 70% of subjects in a wide variety of clinical research studies may suffer from a therapeutic misconception (Lidz et al. n.d.).

When present, a therapeutic misconception vitiates the ethical basis for deviation from clinical norms in research settings. That is, insofar as the justification for a departure from the principle of personal care is premised (at least in part) on the subject’s knowing relinquishment of an entitlement to a physician’s undivided loyalty, a subject’s failure to appreciate that this is occurring renders consent invalid. Thus, one of the most important concepts to be communicated to prospective research subjects is precisely how the study to which they are being asked to consent differs from what they would encounter in an ordinary clinical setting. Why is this so difficult for subjects to grasp?

Undoubtedly several factors combine to obscure in subjects’ minds the differences between ordinary clinical treatment and research involvement. A lifetime of experience in clinical settings has often rather firmly entrenched the notion that physicians ought to be single-mindedly devoted to advancing one’s health. But another part of the problem almost certainly arises from the discussions that subjects have with the researchers themselves. Some researchers may deliberately attempt to deceive potential subjects about the personal benefit to be obtained from joining a research study, but I suspect that the number of such reprobates is small. More significant, I believe, is the confusion that exists in the minds of the researchers themselves regarding the differences between rendering treatment in clinical and research settings.

One need only talk with clinical researchers to hear frequent assertions that the care they provide is at least as good as—if not better than—the care subjects will receive in the nonresearch clinic down the hall. These claims are important to many researchers, because they themselves do not fully understand the differing ethical frameworks that govern their behavior in the clinic and in the research unit. Often feeling bound to continue doing the best they can for the patients who enter their studies, they work hard to persuade themselves and their potential subjects that this will, in fact, be the case. The result is that everyone ends up confused. Researchers and subjects alike fail to distinguish the benefits and risks of research from those that obtain in ordinary treatment. One might say that both groups fall prey to a therapeutic misconception.

If we are to disabuse research subjects of unrealistic beliefs regarding the therapeutic benefits of participating in studies, surely we must first take the same step with the researchers themselves. So long as the line remains blurry as to the obligations that physicians must discharge in each setting, that task will be impossible. Were placebo use to be proscribed in clinical research because it provides fewer clinical benefits than partially effective treatment, we would be reinforcing the confusion between the ethics of clinical care and the ethics of clinical research. Confused investigators generate confused subjects; the latter then enroll in studies, seeking therapeutic benefits that are almost certain not to accrue.

Thus, the analysis offered by Miller and Brody has the very happy side benefit of helping researchers to understand more clearly how distinct are the ethical obligations associated with research. To the extent that they grasp this, they are more likely to be able to communicate the distinctions to their subjects, with the latter perhaps thereby enabled to make decisions about participation that more closely reflect a valid assessment of risks and benefits. A little bit of clear thinking goes a long way.

References