

## Ignorance and Altruism

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The trade-off between a present case and less tangible, but equally real and important, future cases represents a classic ethical dilemma. Is it appropriate to do less than we can for a needy patient, investing the savings in a program that might help many in the future? For a physician who engages in both clinical practice and research, a version of this dilemma might seem to appear in the form of a conflict between the roles of personal caregiver and scientist, the one whose commitment is to the needs of the present patient and the other who, by contributing to knowledge, seeks to serve the more general good.

Although the dilemma may well be unresolvable in general, it should not be a factor in the clinical decisions of the physician-scientist. As Maurie Markman concludes in "Ethical Difficulties with Randomized Clinical Trials Involving Cancer Patients," "Above all, the physician's responsibility is to the individual patient, and the need to increase knowledge to improve the lot of future patients must always take second place." Here there is no dilemma--the interests of the present patient must prevail.

But a problem remains--Markman's conclusion is often interpreted as meaning that physicians should participate in a randomized clinical trial only when they truly have no preference for either treatment. This

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would represent a severe handicap to medical progress. Important trials are sometimes conducted by the proponents of a new therapy, who see the randomized trial as the most effective way to convince skeptics and thereby to improve patient care. And it is certainly true that many if not most physicians who participate in randomized clinical trials--while not sure which treatment will turn out to be better--have a definite opinion. If their participation were prohibited, then many fewer trials could be done.

I would like to suggest that the priority of the patient's interests does *not* imply that a physician who has a treatment preference should not take part in a randomized clinical trial. What it does imply is that the physician should enroll only those patients who make a truly informed choice to participate. The ethical basis for the trial rests not on how well the physician's treatment preference approximates the fragile state known as "equipose",<sup>1</sup> but on how well informed and autonomous is the patient's choice. That is, it rests not on the physician's ignorance, but on the patient's altruism.

The generic problem is this: To investigate the relative merits of treatments *A* and *B*, a study will be done in which some patients will receive *A* and some *B*. Which treatment an individual patient receives will be determined at random. The reason for random treatment assignment is to enhance the scientific credibility of the results (by eliminating selection bias, for example). The ethical problem is that the physician is allowing a coin toss to replace his clinical judgment in

choosing the treatment for this patient.

Markman's presentation, like most discussions of this problem, focuses on the physician's state of knowledge--what he believes and on what he bases his opinions ("If this were your wife/mother/sister, what would you recommend?"). The question that is asked is whether he can ethically enroll in the study a patient for whom he believes, for one reason or another, that *B* is the better treatment. To Sir Austin Bradford Hill, a pioneering proponent of randomized clinical trials, the answer was an unqualified "No":

If the doctor . . . thinks even in the absence of any evidence that for the patient's benefit he ought to give one treatment rather than the other, then that patient should not be admitted to the trial. Only if, in his state of ignorance, he believes the treatment given to be a matter of indifference can he accept a random distribution of patients to the different groups.<sup>2</sup>

This position would seem to preclude the physician's participation in the trials described by Markman.

But others argue that at times the physician need not act according to his beliefs.<sup>3</sup> Benjamin Freedman, for example, considers a situation in which experts disagree about the preferred treatment. Investigators with a decided preference for *B* propose to conduct a randomized clinical trial.

The ethics committee asks the investigators whether, if they or members of their families were within the [study] population . . . they would not want to be treated with . . . *B*? An affirmative answer is often thought to be fatal to the prospects for such a trial, yet the investigators answer in the affirmative. Would [such] a trial . . . be ethical?

I believe that it clearly is ethical. . . . The ethics of medical practice grants no . . . meaning to a treatment preference, however powerful, that is based on a hunch or anything less than evidence publicly presented and convincing to the medical community.<sup>4</sup>

This sort of epistemological argument tries to avoid Hill's sweep-

ing conclusion by distinguishing between beliefs that are supported by sound scientific evidence and/or a solid professional consensus, and beliefs that are not--between competent medical judgments and personal hunches.<sup>5</sup> The solution to our problem is not to be found in such distinctions. This is shown in Markman's second example, where the Mayo Clinic investigators of combination chemotherapy apparently have treatment preferences that are not widely shared today. But do those preferences not represent competent medical judgments? Competent professionals can disagree, and one's judgment is not reduced to a mere hunch by the fact that a respected colleague has a different opinion. The "evidence publicly presented" can be convincing to some members of the medical community and not to others. Still, treatment decisions have to be made, and each physician must treat his patients according to his own best professional judgment. In fact, it may be that his judgment is most important precisely in those situations of greatest uncertainty, where not everyone would necessarily reach the same conclusion.

If the physician must use his best professional judgment, even when that judgment does not command unanimous assent, and even when he himself is not absolutely certain that it is correct, then when can he ethically allow that his patient's treatment be chosen at random? Only in those rare cases where he is utterly diffident? No. Random choice is ethical when the informed autonomous patient freely elects to have his treatment selected in that way.

The physician might explain to the patient that treatments *A* and *B* are being compared and that, although he is not sure, he suspects that *B* will prove to be better. He might also point out that some of his colleagues prefer *A*. In such

circumstances, many patients will choose to behave altruistically, volunteering to take part in the study for the benefit of future patients.

The patient makes a transaction. He gives up something to which he is entitled, namely that his treatment will be chosen according to his and his physician's best judgment (uncertain, as all judgments are) about what is best for him. In return, he gains the satisfaction of contributing to an enterprise that he judges worthwhile. Many of us would happily volunteer for a randomized trial of a new analgesic versus a placebo for mild pain. But even treatments for critical illness can be compared in a randomized clinical trial. What is required is not physicians without opinions, but patients who, aware of the uncertainty, judge that what they are giving up in personal care is less important than what they will gain in personal satisfaction. In fact, taking part in such a trial can be a way for the patient to turn a difficult predicament into something meaningful, an opportunity to help others with similar problems. The decision is the patient's, not the physician's.

When medical care is viewed under the paternalistic model, with the physician acting on behalf of the passive and dependent patient, randomized clinical trials are indeed problematic. Only in some very special cases, such as Markman's first example, where the preferred therapy is available only to those who take part in the trial, can randomized trials avoid ethical difficulties. But under the model of the autonomous patient who--with the help and advice of the physician--makes his own choices, ethical justification of random treatment assignment is possible. That justification does not rest on whether the physician has a preference or on how a preference might be justified. It rests on the concept of patient

autonomy and an adequate process of informed consent.

If this view is accepted, then ethical arguments about whether a randomized trial should be done, or which physicians can take part, are replaced by practical questions, such as "Will enough patients choose to participate?" (maybe so, in Markman's example of combination chemotherapy; probably not, in his example of surgical debulking of ovarian tumors) and "Will those who do participate be such a special group that it will be impossible to project findings to a more general patient population?"

An autonomous adult can elect to make a sacrifice for the benefit of society. But can a guardian elect for a child to make such a sacrifice? What about the adult patient who adopts an attitude of dependence, one for whom the physician must play a paternalistic role? These and other hard questions remain. They might identify areas where randomized studies are not appropriate. But ethical justification for randomization can often be found when the focus shifts from what the physician thinks to what the patient wants.

## NOTES

1 C. Fried, *Medical Experimentation: Personal Integrity and Social Policy* (Amsterdam: North-Holland, 1974).

2 A.B. Hill, "Medical Ethics and Controlled Trials," *British Medical Journal* 1 (1963): 1043-49.

3 D.P. Byar, R.M. Simon, W.T. Friedewald, et al., "Randomized Clinical Trials: Perspective on Some Recent Ideas," *New England Journal of Medicine* 295 (1976): 74-80; M.E. Freund, "Surgical Research," in *Human Subjects Research*, ed. R.A. Greenwald, M.K. Ryan, and J.E. Mulvihill (New York: Plenum Press, 1982), 169-79; B. Freedman, "Equipose and the Ethics of Clinical Research," *New England Journal of Medicine* 317 (1987): 141-45.

4 Freedman, "Equipose," 144.

5 R.M. Royall, "Ethics and Statistics in Randomized Clinical Trials," *Statistical Science* 6 (1991): 52-88.