Sounding Board

How to Resolve an Ethical Dilemma Concerning Randomized Clinical Trials

An apparent ethical dilemma arises when physicians consider enrolling their patients in randomized clinical trials. Suppose that a randomized clinical trial comparing two treatments is in progress, and a physician has an opinion about which treatment is better. The physician has a duty to promote the patient's best medical interests and therefore seems to be obliged to advise the patient to receive the treatment that the physician prefers. This duty creates a barrier to the enrollment of patients in randomized clinical trials.[1-10] Two strategies are often used to resolve the dilemma in favor of enrolling patients in clinical trials.

THE "EITHER YOU KNOW WHICH IS BETTER OR YOU DON'T" STRATEGY

According to one strategy, physicians should not recommend one treatment over another if they do not really know which one is better, and they do not really know which treatment is better in the absence of data from randomized clinical trials.[11] Data from uncontrolled studies are often influenced by the desire on both the investigator's part and the patient's part to obtain positive results.[12] Journal editors are more likely to publish reports of studies with positive results than reports of studies with negative results.[13] A treatment recommendation based on weaker evidence than that obtained from a randomized clinical trial is like a recommendation based on a mere hunch or an idiosyncratic preference.[14] Thus, according to this argument, in the absence of data from a randomized clinical trial, evidence that provides an adequate basis for recommending a treatment rarely exists, and the enrollment dilemma is based on a mistake.

This strategy for resolving the dilemma is simplistic. It assumes that evidence available to physicians can be only one of two kinds: gold-standard evidence or worthless prejudice. But clinical judgments may be based on evidence of intermediate quality, including physicians' experience with their own patients, their conversations with colleagues concerning their colleagues' experience, their evaluation of the results of nonrandomized studies reported in the literature, their judgment about the mechanism of action of one or both treatments, or their view of the natural history of a given disease. Evidence need not be conclusive to be valuable; it need not be definitive to be suggestive. Because all good physicians allow evidence of intermediate quality to influence their professional judgment when a relevant randomized clinical trial is not being conducted, it is unreasonable to claim that such evidence has no worth when a relevant randomized clinical trial is being conducted. Therefore, the "either you know which is better or you don't" strategy for dealing with the enrollment dilemma is not persuasive.

ADOPTING A LESS STRICT THERAPEUTIC OBLIGATION

The dilemma about enrolling patients in randomized clinical trials is generated by the claim that a physician has a strict therapeutic obligation to inform the patients of the physician's treatment preference, even when the preference is based on evidence that is not of the highest quality. The dilemma could be resolved if the physician's therapeutic obligation were less strict. This strategy was developed by Freedman.[14,15] He argued that the standard for determining whether a physician has engaged in medical malpractice or committed some other violation punishable by a professional disciplinary body is the standard of good practice as determined by a consensus of the medical community. There is no consensus about which of two treatments being compared in a randomized clinical trial is superior. (Otherwise, why conduct the trial?) Therefore, enrolling a patient in the trial does not violate the physician's therapeutic obligation to the patient, regardless of the physician's treatment preference. In addition, a patient who consults a physician with a preference for treatment A could have consulted a physician who preferred treatment B. Therefore, enrolling a patient in a randomized clinical trial in order to be randomly assigned (perhaps) to treatment B does not make such a patient worse off than he or she would otherwise have been.

Despite these points, compelling arguments for the stricter interpretation of therapeutic obligation remain. In the first place, consider what physicians expect when they seek professional advice from their malpractice attorneys, their tax advisors, or for that matter, their own physicians. Surely they expect — and believe they have a right to expect — not merely minimally competent advice, but the best professional judgments of the professionals they have chosen to consult. In the second place, patients choose physicians in order to obtain medical advice that is, in the judgment of those physicians, the best available. If physicians do not provide such advice, then they tacitly deceive their patients, unless they disclose to their patients that they are not bound by this strict therapeutic obligation. Physicians should adopt the strict therapeutic obligation.

A RESOLUTION

The clash between a strict therapeutic obligation and a less strict one is only apparent. On the one

hand, the less strict therapeutic obligation is supported by the argument that it is morally permissible to offer to enroll a patient in a randomized clinical trial. On the other hand, the strict therapeutic obligation is supported by the arguments concerning treatment recommendations. Recommending is different from offering to enroll. A recognition of this difference provides the basis for a solution to the dilemma.

Suppose that a randomized clinical trial is being conducted to compare treatments A and B and that a physician prefers A and informs the patient of this preference. All physicians have an obligation to obtain their patients' informed consent to treatment. A physician has respected this right only if he or she explains to the patient the risks and benefits of reasonable alternatives to the recommended treatment and offers the patient an opportunity to choose an alternative, if that is feasible. Either treatment B or enrollment in the trial comparing A and B is a reasonable alternative to treatment A, because presumably, A is not known to be superior to B. Indeed, there is some evidence that enrollment in a randomized clinical trial is a superior therapeutic alternative when a trial is available.[16] Respect for a patient's values is a central purpose of informed consent. A particular patient may place a greater value on participation in a study that will contribute to medical progress and to the well-being of patients in the future than on the unproved advantages of following the physician's recommendation. Therefore, a physician can both recommend a treatment and ask whether the patient is willing to enroll in the randomized clinical trial.

This resolution is based on the recognition that there can be evidence of the superiority of a treatment that falls short of the gold standard for evidence but is better than worthless. It also takes into account the good arguments for the view that physicians have a strict obligation to recommend the best treatment on the basis of their professional judgment, even when the recommendation is based on evidence that falls short of the gold standard. Nevertheless, because all physicians have an obligation to take informed consent seriously, because respect for informed consent entails offering a patient the reasonable alternatives to the recommended treatment, and because enrollment in an appropriate randomized clinical trial is often a reasonable therapeutic option, one could argue that offering a patient the opportunity to be enrolled in a clinical trial is not only morally permissible but, in many cases, also morally obligatory, if a relevant trial is being conducted and if enrollment in it is feasible. Taking informed consent seriously resolves the dilemma about whether to enroll patients in randomized clinical trials.

Is this analysis clinically realistic? Some may argue that if clinicians inform their patients that they prefer treatment A, then few of their patients will consent to participate in a trial comparing A with B. Furthermore, many clinicians may be unwilling to invest the time necessary to explain the option of enrollment in a trial, particularly if it seems unlikely that a patient, knowing the physician's preference for one of the treatments, will choose to participate in the trial.

On the other hand, in recent years the public has been exposed to a barrage of medical information and misinformation. Explaining to patients the difference between solid scientific evidence of the merits of a treatment and weaker evidence of its merits is worthwhile, whether or not a relevant randomized clinical trial is being conducted. When a relevant trial is being conducted, offering the patient enrollment in the trial should not impose on the physician a large, additional burden of explanation. Physicians can promote enrollment by explaining that their preference is based only on limited evidence, which may or may not be reliable. They can also explain that data from randomized clinical trials have often shown that the initial studies of new treatments were overly optimistic.[17]

In addition, using this informed-consent strategy to resolve the enrollment dilemma may not be morally optional. My analysis is based on two important obligations of physicians. The first is the strict obligation to recommend the treatment that is, in the physician's professional judgment, the best choice for the patient. The second is the obligation to obtain the patient's informed consent to the recommended treatment. The duty of obtaining informed consent implies that the physician is obligated to offer the patient the opportunity to enroll in a clinical trial when one is available, even if the physician has a treatment preference. The physician owes this duty to the individual patient, not simply to future patients who may benefit from advances in medical knowledge. Thus, the informed-consent strategy for resolving the dilemma about enrolling patients in randomized clinical trials leads to the conclusion that physicians have a greater duty to offer their patients enrollment in trials than has previously been realized. A strict, thoroughly defensible, therapeutic obligation need not interfere with the conduct of randomized clinical trials.

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