EDITORIAL

Why Community Physicians Should Encourage Their Patients to Participate in Randomized Clinical Trials

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IN THE PAST DECADES an alphabet soup-like avalanche of large-scale cardiovascular clinical trials — CDP, AMIS, PARIS, MRFIT, USPET, HDFP, LRC, NEHDP, BHA, and more — has taken place. The critical need for participation of both the physician and the patient in these trials make it timely to review the benefits to the patient, to the referring physician, and to society as a whole.

Randomized controlled clinical trials are often the only means of evaluating the relative efficacy of methods of medical and/or surgical treatment (this relates both to "established" forms of therapy and to new modalities of management), and for evaluating ways of preventing cardiovascular disease. Ethical considerations require that, before the institution of a clinical trial, neither of the alternative forms of management being tested is obviously superior to the other, and that neither is associated with undue side effects or risks; thus, the concept of randomization is most appropriate and must be explained by physicians to their patients.

All patient volunteers enrolled in clinical trials have detailed medical supervision, in addition to that provided by their primary physicians. The comprehensive clinical and laboratory examinations (as well as those done at follow-up visits) may reveal unsuspected and, at times, remediable disorders. The surveillance during the trial, without cost, may be a major tangible benefit to the participating patient.

The primary physician, nonetheless, may have legitimate concerns about the participation of an individual patient. Will enrollment and participation in a clinical trial be of value, constitute a nuisance, or even be detrimental to a specific patient? Often, the individual and group sense of involvement, of helping and commitment, boost the participating patient's ego strength. The compulsive, precise patient is characteristically impressed with and encouraged by the detailed organizational components of the trial; the anxious patient is reassured by the precision and breadth of surveillance; and the controlling or managing patient derives satisfaction from his ability to contribute. Voluntarism, characteristic of American society, gives the participating patient a chance to contribute to the welfare of the population in general. In addition, the patient may, in the future, benefit directly from the results of the trial in which he participated or from the results of other clinical research efforts that deal with his medical problem.

Clinical trials provide the physician with reliable evidence of the relative merits of therapeutic regimens. The physician has a responsibility to determine objectively, not merely by opinion or anecdotal evidence, the optimal modality of care for his patient; clinical trials provide the means to subject new information about therapy to careful, systematic evaluation, weighing both the assets and the liabilities of each treatment.

However, community physicians often have valid concerns about whether the clinical trial, overall, is appropriate; or whether enrollment of a particular patient in a specific trial is appropriate. Those responsible for the design of clinical trials should encourage each referring physician to communicate or meet with the senior investigator at the participating center, who can discuss and detail the conflicting or inadequate...
data which the trial was designed to resolve. A decision to embark on a clinical trial requires that the problem be of sufficient importance and magnitude to warrant the significant expenditure of skilled personnel, time and funds; that the character of the information gap or conflict be such that it can be expected to be best resolved in the context of a trial; and that there be a reasonable anticipation that the trial will, indeed, generate data adequate for clinical decision-making. Typically, this information can reassure the physician that there is a need for the trial, that it is worthy of his participation and the participation of his patients; and it should encourage him to invest the necessary time and effort to select and counsel with patients who will meet the criteria for entry into the study. This contact with the investigative center should be the initial link between the referring physician and the study, which will be augmented as the study proceeds by the sharing of information both relative to the participating patient and to the progress of the trial in general.

The physician may be apprehensive about losing a patient or relinquishing control of a patient entered into a clinical trial. The patients participating in clinical trials remain under the care of the primary physician, with patients referred for management to their own physician for new medical problems arising or detected during the clinical trials. Naturally, the referring physician should receive not only copies of the patient record pertinent to the trial, but also general scientific information about the trial as well.

The contributing doctor is an important part of the clinical trial, both because of his role in identifying the patient as appropriate for the trial and his encouragement of the patient's continued participation. Day-to-day monitoring and analyses of data in the course of a clinical trial assure that once unquestionably favorable evidence has accrued to one regimen or excessive risk appears related to another, the trial cannot ethically continue and will be terminated. The final results of the trial should favorably affect the referring physician’s plan of care for the participating patient and for his other patients with a comparable clinical problem. For example, in the Coronary Drug Project, a study assessing the efficacy of cholesterol-lowering drugs in altering the mortality of men recovered from myocardial infarction, both high- and low-dose estrogen regimens were associated with a greater mortality than placebo treatment. Removal of these two regimens from the clinical trial and rapid dissemination of this information both to the referring physicians and to the medical community in general, hopefully resulted in a significant change in clinical practice. Presumably, the management of hypercholesterolemic patients after myocardial infarction was altered, resulting in the saving of lives.

Clinical trials are designed to improve health care outcomes and reduce health care costs. Because cardiovascular diseases cost our nation over $40 billion last year, even the huge expenditure for large-scale clinical trials may prove cost-effective. Data from well-designed clinical trials contribute to improved management of the patient with hypertension, coronary atherosclerotic heart disease, etc. For example, the data base for the current management of severe, moderate and mild hypertension derives from the several Veterans Administration controlled clinical trials, documenting a decrease in morbidity and mortality in the treated population of hypertensive patients. Another controlled trial, the Coronary Drug Project, identified that several lipid-lowering agents, at that time in general clinical use to manage hypercholesterolemia in coronary patients, did not improve the mortality rate in men who had recovered from a myocardial infarction. These and other data, by identifying optimal modes of management and by defining therapies without demonstrable efficacy or with increased risk, have exerted a major impact on medical care practices.

Ongoing controlled trials are designed to provide the clinician with answers to dilemmas encountered daily in clinical practice. For example, does aspirin (AMIS) or persantine (PARIS) alter the natural history of the postinfarction patient? What is the appropriate status of propranolol (BHAT), of prescriptive exercise (NEHDP) in the care of these patients? Does coronary risk factor modification (MRFIT) improve the outlook for the coronary-prone individual?

Because the pattern of care of the patient is based on information derived from previous patients with the same medical problem, current patients should understand their moral obligation to the welfare of future patients. A patient’s participation in a clinical trial encourages others to participate, augmenting the potential benefits from advancing medical knowledge which may help the individual patient, members of his family, future patients with the disease, etc. Society gains if health care is economically improved by better modalities of treatment or improved methods of disease prevention; society, as a whole, may lose significantly if physicians and their patients do not help to evaluate new methods of care and prevention by ethical, meticulous, comprehensive, unbiased clinical trials.

The referring physician serves as a pivotal force in this complex interaction — critically assessing the proposed clinical trial, meticulously selecting patients appropriate for entry into a study and counselling them regarding their participation; relating in an ongoing manner to the investigative center and the available study data; and subsequently fulfilling personal and societal responsibilities by incorporating the newly-generated information into an improved plan of care for his patients.
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