Industry-sponsored clinical trials: The problem of conflicts of interest

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A pharmaceutical company invites a surgical oncologist at an academic medical center to participate in an industry-sponsored clinical trial of a novel adjuvant chemotherapy agent designed for use in the perioperative period. The protocol drug is in a phase III trial and is being compared with the standard chemotherapeutic adjuvant. The pharmaceutical company offers to reimburse the physician $500 per patient enrolled in the trial. The pharmaceutical company needs the physician to enroll 200 participants in a 12-month period.

This case illustrates a common conflict of interest in the practice of clinical medicine and surgery. A conflict of interest occurs when a primary professional responsibility is compromised, consciously or unconsciously, by a secondary interest. Because the surgeon in this example is eligible to receive significant monetary compensation for enrolling patients in the clinical trial, it may be difficult to remain focused on patient interests when explaining the purpose, risks, benefits, and rationale for the clinical trial to patients. Thus, the conflict of interest in this case is between the physician's potential financial gain and his or her fiduciary duty to patients.

This article analyzes four possible options to respond to this ethical dilemma:

1. Participate in the clinical trial, accept the reimbursement, and disclose only the standard details of the trial to participants during discussions relevant to informed consent
2. Participate in the clinical trial, accept the reimbursement, and include the reimbursement arrangement when disclosing the details of the trial to participants
3. Participate in the clinical trial without accepting the reimbursement
4. Do not participate in the clinical trial

Option 1

Participate in the clinical trial, accept the reimbursement, and disclose only the standard details of the trial to participants during discussions relevant to informed consent. This course of action allows the surgeon to give potential enrollees the option of either participating in the clinical trial or receiving standard treatment. The physician assumes the patient has the capacity to make an informed decision about the choices based on his or her knowledge of all possible therapeutic options, including the drug in Phase III trial. The patient must understand the clinical significance and personal consequences of enrolling in a Phase III trial. As a patient's trusted and oftentimes sole source of medical information and advice, the physician has the responsibility to educate and guide patients to a safe and suitable medical decision. In doing so, the physician must avoid or properly manage bias when disclosing all relevant information about the treatment options presented to ensure that the patient is making an informed and autonomous decision.

The primary problem with this approach is the added difficulty the surgeon faces in avoiding or managing potential bias when presenting information about trial participation. It will be tempting for the physician to rationalize the benefit of the trial drug or to underestimate the risk for adverse reactions. In a systematic review of the literature evaluating industry sponsorship of clinical trials, Golder and Loke noted that researchers involved in pharmaceutical-sponsored trials significantly minimized the risks associated with enrollment.[1] Because many trials pay investigators on a per capita basis, participating physicians have a significant incentive to enroll a large number of patients. Reimbursement rates are not standardized, leaving each participating physician to consider where to draw the line between reasonable and excessive compensation. Disproportionate reimbursements heighten the incentive to recruit overzealously and thereby to jeopardize physician nonpartisanship, data integrity, and patient safety and autonomy.

Option 2

Participate in the clinical trial, accept the reimbursement, and include the reimbursement arrangement when disclosing the details of the trial to participants. The standard practice of informed consent requires that clinical trial participants be given adequate information to make informed and autonomous decisions. The reimbursement amount per enrollee in this case begs the question: "Can a potential participant's autonomy be respected without disclosure of the reimbursement amount and purpose?"

To address this concern and better respond to the conflict of interest created by per capita reimbursement, this option calls for the surgeon to disclose the reimbursement arrangement to participants, with explicit information about the potential personal gain available to the physician that would surpass the basic costs of drug treatment and patient care. Disclosing the reimbursement arrangement sterilizes the conflict of interest and shifts to the patient the task of determining the extent to which financial consideration is biasing the information that the physician provides.

This option calls for the patient to competently integrate the reimbursement information into the decision-making process. A review by Licurse and colleagues found that patients favored the disclosure of their physicians' financial ties and, more importantly, an oversight committee to monitor and safeguard patient interests.[2] This review suggests that patients recognize their limitations with regard to making informed decisions, especially in light of their inexperience with pharmaceutical industry proceedings. Sah noted that patients made decisions erratically when provided with the information of their physician's financial gains and introduced the idea of "burden of disclosure" to describe the increased pressure to comply with a physician's recommendation after a disclosure has been made.3 Patients struggle with reimbursement information, with many preferring to depend on an oversight body to assess and clarify these ethical and logistical issues.

This second option may create more confusion among potential trial participants, rather than improve the informed consent process. Also, it would be a mistake to assume that pharmaceutical companies will have robust and independent internal review boards. Disclosure of the reimbursement arrangement illuminates but does not eliminate conflict of interest.

Option 3

Participate in the clinical trial without accepting the reimbursement. By eliminating the financial conflict of interest in this case, this option maintains the patient's autonomy by greatly reducing the risk of physician bias in recruitment. Without a need to disclose financial ties to the industry study sponsor, this option protects the physician's trusting relationship with the potential participants.
However, conflicts of interest extend beyond financial gain. In many cases, physicians named as the primary investigator of a drug study may be credited with authorship for publication of positive studies. This additional incentive creates a range of disclosure quandaries similar to those associated with the reimbursement arrangement in this case. A physician in this situation may subconsciously exaggerate the benefits of the study, as was found to be the case in numerous studies across subspecialties.[4] Industry-funded research tends to have more positive results, and the primary investigators of such studies tend to overstate the benefits and underestimate the harms of the protocol drug.[4]

While this option does potentially eliminate the bias associated with financial gain, the physician would have to justify participating in a research study without reimbursement to offset costs. Research protocols require a significant amount of additional work from physicians and ancillary staff. A lack of reimbursement could be a disincentive for clinicians to participate in clinical trials.

Option 4

Do not participate in the clinical trial. The action most consistent with the ethical principle of nonmaleficence is to refuse participation in the clinical trial. This option resolves the ethical issues of conflicts of interest between patient care and personal gain and ensures that the physician does not subject patients to any additional risk.

However, without clinical trials to test new treatments, the potential for discovery or refinement of new ideas and, thus, for treating patients in the future with more effective and appropriate medications will be forestalled.

Ethical bottom line

Industry has become increasingly involved in medical research—initiating clinical trials, sponsoring investigator patient recruitment, and often providing medications to patients who may not otherwise have access to treatment.5 Such involvement creates legitimate concern about conflicts of interest for physicians as they recruit for and assist with the implementation of industry-sponsored clinical trials. This concern is most acute when the participating physicians receive reimbursements that clearly cross the line between reasonable and excessive compensation.

Most academic medical centers have general guidelines for monitoring research revenue.6 The guidelines are less clear in community practice centers. They may not have ethics boards for monitoring the reimbursement arrangements of pharmaceutical-sponsored clinical trials. Such boards have no standard reimbursement rate for patient enrollment. Without specific monitoring teams in place, physicians are left to consider each research trial individually and to exercise self-discipline.

Physicians have an obligation to place the well-being of their patients before personal or professional gain. This obligation trumps the need to contribute to medical advancements or drug development. Patients ought to be in a position to decide whether to enroll in a clinical trial. They need to and should be in a position to trust their physicians to be impartial when presenting the information upon which they make these important decisions.

A primary task of the physician is to balance protecting the patient's autonomy with offering treatments in which the benefit outweighs risks in an acceptable proportion. Many patients take their physician's recommendations without serious reservations, though these recommendations are taken to represent independent judgments. Whereas patients always have the option of seeking a second opinion, at least in theory, they do not routinely pursue this course of action. Accordingly, it is crucial that physicians provide information in as unbiased a manner as possible when presenting treatment options to their patients. Before agreeing to enroll patients in an industry-sponsored clinical trial with significant financial compensation, physicians would do well to ask themselves, "Can I explain/justify the reimbursement arrangement to a respected colleague, to the nurse with whom I have worked for many years, or to an admiring medical student?"

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