

SOUNDING BOARD

Disclosure of Financial Relationships to Participants in Clinical Research

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In keeping with previous statements by a number of prominent groups,¹⁻⁴ the Institute of Medicine has recently stressed the need for vigilance in managing conflicts of interest to ensure the integrity of clinical research.⁵ The Institute of Medicine adopts a position similar to that of the Association of American Medical Colleges¹ — that is, it assumes that there is a rebuttable presumption of a conflict of interest if the investigator has a financial interest in the outcome of research that involves human subjects. Although the institute's report emphasizes the need for disclosure of financial interests to institutions and peer reviewers, it differs from many of the earlier guidelines in that it stresses the need to limit researchers' financial interests more than the need to disclose such interests to research participants.

Nevertheless, at times such disclosures may be called for. In some cases, the relevant institutional body will conclude that a potential conflict of interest is tolerable. In others, it might view a financial relationship as not posing any conflict of interest (e.g., the study sponsor's paying an investigator for the costs of conducting a study). Finally, bans on financial relationships with trial sponsors are only recommended, not required, so some institutions might still allow them. In all three of these circumstances, it may be reasonable to expect that — at a minimum — disclosure to the research subjects would be required.

Sound management of conflicts of interest should be based on clear policy goals and, whenever possible, rely on valid empirical data.⁶ To help researchers better understand the proper role of disclosure to trial participants as one of several techniques for managing conflicts of interest, we draw on 5 years of empirical data from the Conflict of Interest Notification Study, which

was supported by the National Institutes of Health, as well as from other research findings, to formulate six suggested goals of disclosure.

GOALS OF DISCLOSURE

Policymakers and officials charged with oversight of human subjects may consider several different goals when deciding whether to require that financial relationships be disclosed to potential research participants. We discuss six possible goals of such disclosures (Table 1).

PROMOTING INFORMED DECISION MAKING

Disclosures to research participants during the informed-consent process are meant to promote autonomous decision making.⁷⁻⁹ What exactly constitutes an autonomous decision by the participant is a matter of debate, but most experts describe it as a choice made after the person has gained a substantial understanding of the potential risks and benefits of enrollment.

Studies have identified at least four major challenges to achieving a substantial understanding of financial relationships in clinical research. First, there is wide variation in views and practice about what to tell participants about a researcher's financial relationships.⁹⁻¹³ A typical disclosure statement identifies the possibility of a bad clinical outcome, usually based on data from preliminary studies in animals or humans. Financial disclosures present two principal risks: harm to the research participants and harm to the study's scientific integrity (e.g., the investigator might be biased in interpreting the results). These risks are more difficult to estimate than medical risks, because we lack data for estimating the risks and also for explaining how an investigator's financial relationships might best inform a participant's decision whether to enroll in a trial.

Table 1. Potential Goals and Challenges of Disclosing Financial Relationships in Clinical Research.

Goal	Challenges
Promoting informed decision making	There is no empirical basis for estimating the risks of a bad clinical outcome arising from financial relationships; some participants lack sufficient background or experience to understand the financial relationships in clinical research or require extremely lengthy explanations; disclosing that the investigator invested in an experimental intervention could inflate some patients' perception that the intervention might directly benefit them; those who are designated to obtain informed consent do not always have enough information to answer study participants' questions.
Respecting participants' perceived right to know	Determining what people really want to know is methodologically difficult; selecting the content of disclosure forms on the basis of what people want to know could lead to misleading or unrealistically long consent documents.
Establishing or maintaining trust	Disclosure could either undermine or promote trust, depending on the type of financial relationship in question.
Minimizing risk of legal liability	Disclosure is not required by law in some states; where there is a risk of legal liability, disclosure may not provide sufficient protection.
Deterring troubling financial relationships	There are no data to indicate whether disclosures deter investigators from entering into potentially troubling financial relationships; disclosure might give the investigator moral license to behave in a biased manner.
Protecting research participants' welfare	There is no clear evidence that the welfare of research participants is threatened by investigators' financial interests; disclosure can protect participants' welfare only through improved informed decision making or deterrence of unacceptable relationships.

Another challenge is that many people have trouble understanding the nature and implications of financial relationships in clinical research. For example, in focus groups, some participants remained confused about certain financial interests — especially equity interests — even after 2 hours of discussion.¹⁴ Others mentioned that before the focus group, they would not have known what to ask about such relationships if given the opportunity — both because they might not have understood the information and because they might not have considered these relationships important. If people do not understand a topic well enough to ask questions, they will find it difficult to reach a substantial understanding. These problems are also probably exacerbated by the daunting length and complexity of many consent documents.

A third challenge is the possibility that disclosure will paradoxically reinforce a “therapeutic misconception” — namely, blurring the distinction between clinical care and clinical research.¹⁵⁻¹⁷ Data suggest that some people place more faith in an experimental intervention when the investigator has a financial stake in the product being tested, believing that the investigator's investments signal his or her confidence in the product.¹⁴ The failure to comprehend the risks associated with financial interests raises ques-

tions about whether financial disclosures contribute positively or negatively to informed decision making.

Finally, study coordinators, who are frequently charged with obtaining consent, often lack the information they need about investigators' financial relationships. In one survey, over 75% of study coordinators cited this deficit as the primary barrier to addressing participants' questions about conflicts of interest.¹⁸

These four challenges make it difficult for disclosures of financial interests to promote the informed and substantial understanding that should be the basis for a participant's autonomous decision about whether to enroll in a clinical trial. As the Institute of Medicine concluded,⁵ “it is not clear that it is reasonable to expect the average participant to understand these issues.”

Nevertheless, financial disclosures clearly make a difference in some people's decisions, especially when equity relationships are involved. For example, in our study of 470 cardiac patients, 5% of those who were told about a hypothetical investigator's equity interest said they would not participate for that reason alone.¹⁹ Yet other financial interests (e.g., per capita payments from sponsors to investigators) do not seem to generate concern, suggesting that such information could be made more prominent or

accessible to improve a participant's understanding of the role such interests might play in the conduct of the research.

Highlighting an investigator's financial relationships, however, might inappropriately increase their salience relative to other, more important information in the consent document.⁹ If the information about financial interests does not in fact represent a tangible risk, presenting it as such could be misleading or could detract from aspects of the study that are more germane to informed decision making. Although a major concern has been that placing too much importance on a researcher's financial interests will cause potential study subjects to decline to participate,⁹ this concern is not borne out by the available data. Several studies that have used different methods of data collection consistently showed that in most cases an investigator's financial disclosures did not dampen subjects' willingness to participate in research studies.¹⁹⁻²³ This is not to say, however, that financial disclosures do not matter at all.

RESPECTING PARTICIPANTS' PERCEIVED RIGHT TO KNOW

Data from multiple studies confirm that most research participants want to know about the investigators' financial relationships, even though this information may not affect their enrollment decision.^{14,22} Some potential study subjects report that they would be angry if they learned about such a relationship after the fact. In other words, they might feel morally wronged by an investigator's failure to disclose his or her personal financial interests in a trial. Nevertheless, in two large studies that examined enrollment decisions in hypothetical clinical trials, most respondents rated financial disclosure as the least important factor in their decision about whether to participate.^{19,23}

This simple right to know could be seen as a question of materiality. A basic tenet of the informed-consent process is that information considered to be material to a decision must be disclosed.²⁴ For some people, information can be deemed material even if it would not change the decision, although others disagree.²⁵ Potential participants consistently express a desire to be informed about financial interests in clinical studies on the part of the institutions or investigators conducting the research.^{14,22} However,

there are methodologic challenges to finding out what patients really want disclosed. The artificial setting and the manner in which people are asked about their preferences for disclosure might affect their answers (e.g., failing to show how the length of a consent form would change if all the information the participant requested was disclosed in full detail). Moreover, some participants might give what they judge to be a socially desirable response rather than express their sincere preference for disclosure. If these responses are used to determine the content of disclosure, consent forms might become overloaded with disclosures of all conceivable benefits and harms, regardless of their likelihood. As already noted, the link between financial relationships and risks of harm, though undoubtedly of concern to study participants, is tenuous and difficult to estimate at best.

ESTABLISHING OR MAINTAINING TRUST

Another goal of disclosure is to establish or maintain the trust of study participants.^{1,26} In the literature, many statements about trust are normative claims about what merits trust (i.e., trustworthiness) rather than empirical reports of the actual determinants of trust.²⁷ In the context of clinical research, the question of trustworthiness is separable from the question of whether in fact the research enterprise is trusted. Empirically, disclosing financial relationships may promote or decrease trust.^{14,28} Findings depend on the type of financial relationship disclosed. In many cases, such as per capita payments by study sponsors to investigators, disclosure is associated with sustained or slightly increased trust, whereas the disclosure of equity relationships with sponsors has been associated with slightly decreased trust.^{14,19,23} Findings also vary according to the object of trust. Trust is greatest for research institutions, moderate for researchers, and lowest for pharmaceutical companies.¹⁹ Overall, it appears that, for most financial interests in research, the disclosures tested so far do not undermine trust and may even help to improve or sustain trust to a moderate extent. However, equity relationships are more worrisome than are other financial relationships.

MINIMIZING RISK OF LEGAL LIABILITY

Many lawyers and administrators believe that disclosing financial relationships will help limit

legal liability. Yet experience to date suggests that disclosure may be neither necessary nor sufficient for legal protection. There are two competing legal views. According to one view, disclosure of financial interests is necessary to avoid violating an investigator's (or institution's) fiduciary duty to act in good faith to protect the interests of a research participant.^{29,30} The alternative view is that the fiduciary duty applicable to clinical treatment does not apply to research settings^{31,32}; even if it did, some courts hold that there is no breach of fiduciary duty or informed consent by failing to disclose information about the clinician, in contrast to information about the treatment.²⁵ Thus, in some states there may be no liability risk for failing to disclose financial relationships. Even if there is such a risk, there is no precedent for determining whether a particular disclosure is sufficiently thorough. Instead, the lesson from the clinical trial involving gene transfer in which Jesse Gelsinger died is that lawsuits can result in substantial financial settlements even when a disclosure has been made.³³

Moreover, consent forms should not be regarded primarily as documents that can be used to shift or waive legal risks. This view makes neither legal nor moral sense. If harm that can be linked to financial entanglements were to occur, a disclosure of those entanglements might make a lawyer's defense somewhat easier, but it is hard to imagine that such a disclosure would entirely obviate the investigator's or institution's legal and moral responsibility to minimize harm to research subjects.

DETERRING TROUBLING FINANCIAL RELATIONSHIPS

This fifth goal assumes that investigators dislike having to disclose their financial interests in a trial and will avoid relationships that might suggest a conflict of interest.³⁴ At present, there are no data to support this particular claim. However, research in other contexts has illuminated possible psychological effects on the person making the disclosure. Some of the findings are troubling and reveal that professionals might in some cases view compliance with disclosure as a moral license to follow their self-interest.^{35,36} Thus, by laying their cards on the table, investigators might adopt an attitude of *caveat emptor* and become less vigilant in policing their own judgmental biases with regard to enrolling patients, collecting data, interpreting results, and other research

activities. These findings stand in sharp contrast both to the legal view of disclosure, as described above, and to an understanding of the consent process as a beneficial exchange of information between investigator and participant.³⁷

PROTECTING RESEARCH PARTICIPANTS' WELFARE

The final goal of disclosure is the most basic: to protect the welfare of research participants. This goal implies that some financial relationships could increase the risk of harm to the study subjects, although there is no systematic evidence of such a connection in the research setting. If there were, any protection from disclosure would come only as a result of either deterring investigators from entering dangerous financial relationships or improving informed decision making.

CONCLUSIONS AND RECOMMENDATIONS

On the basis of the evidence to date, we offer the following recommendations to investigators, institutional review boards, conflict-of-interest committees, and policymakers. First, study participants should not be the sole decision makers with respect to the acceptable risks of investigators' financial relationships in clinical research. At the very least, institutional review boards and officials charged with research oversight should play a significant role in determining the acceptability of these relationships. Many participants do not have the requisite understanding of clinical studies, investigators' responsibilities, or the nature and potential effects of financial incentives.

Second, disclosure during the consent process should be brief and simple and should allow participants to ask questions. Even though they may not fully understand the implications of financial disclosure, such a dialogue encourages transparency, satisfies many participants' perceived right to know, and may foster trust in research in general.

Third, research participants are sometimes troubled by investigators' equity interests in clinical research. Attempting to manage equity relationships through disclosure to participants is problematic, in part because this type of financial stake seems to have greater potential to reinforce a therapeutic misconception than do other relationships. Therefore, an investigator's equity in-

terests should be limited, if not avoided, rather than simply disclosed.

Fourth, study coordinators and other personnel involved in obtaining informed consent should receive the information and training they need to address questions posed by potential subjects concerning investigators' or institutions' financial relationships.

Fifth, those charged with overseeing potential conflicts of interest in research should be explicit about the goals they hope to achieve and should design disclosure statements accordingly to meet those goals.

The Institute of Medicine's recent report will not put an end to the considerable controversy and policymaking that surround physicians' and medical institutions' possible financial conflicts of interest.^{5,38-43} However, as this overview has attempted to show, it was correct to conclude that disclosure is not the remedy that many seek. Still, disclosure may have positive effects on people's satisfaction with and trust in the research process. As the Institute of Medicine recommends, a coordinated research agenda is needed to craft more effective approaches to managing conflicts of interest.⁵ It is important that this agenda distinguish among the various goals of disclosure that we have enumerated. Only in this way can focused empirical studies generate useful data to help us understand the effects and limitations of various policies addressing the oversight and management of financial relationships in clinical research.

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