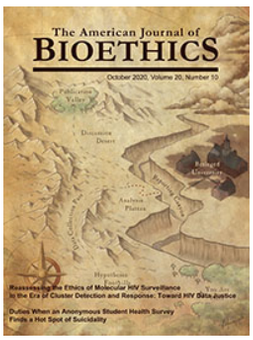

The American Journal of Bioethics

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/uajb20

Inherent Conflict of Interest in Clinical Research: A Call for Effective Guidance

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To cite this article: Marie E. Nicolini & Dave Wendler (2020) Inherent Conflict of Interest in Clinical Research: A Call for Effective Guidance, The American Journal of Bioethics, 20:10, 94-96, DOI: 10.1080/15265161.2020.1806376

To link to this article: https://doi.org/10.1080/15265161.2020.1806376

Published online: 18 Sep 2020.

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THE AMERICAN JOURNAL OF BIOETHICS
2020, VOL. 20, NO. 10, 94–96
https://doi.org/10.1080/15265161.2020.1806376

CASE COMMENTARIES

Inherent Conflict of Interest in Clinical Research: A Call for Effective Guidance

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Clinical research poses a potential conflict of interest between promoting the goals of the research and protecting the interests of the participants (Brody and Miller 2003; Levinsky 2002; Miller et al. 1998). This conflict raises the possibility that researchers' descriptions of the research, as well as their recommendations regarding whether the procedures are clinically indicated, might be influenced by their desire to collect data and thereby contribute to generalizable knowledge. If they are, participants might receive riskier and/or less beneficial interventions than they would have received absent the conflict. For example, Wilfond and colleagues describe a case in which the researcher tells a patient that undergoing surgery as part of the researcher's study is clinically indicated. In that case, it may not be clear whether this opinion is influenced by the researcher's hope of obtaining rare tissue from the patient (Wilfond et al. 2020).

Clinical research exposes participants to risks and burdens for the purposes of collecting research data that might improve care for future patients. Hence, far from being peculiar to a few cases, this potential conflict of interest is inherent to all clinical research. For essentially all studies, the question arises: To what extent are clinician-investigators' descriptions of their research, including the risks, potential benefits, and alternatives, influenced by the goal of generating knowledge to benefit future patients? Given this pervasiveness, and the

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potential to undermine participants' interests, inherent conflicts of interest have received significant attention in the research ethics literature, which notes that, since these conflicts "cannot be eliminated, they must be regulated" (Levinsky 2002).

In our experience, the enormous attention paid to inherent conflicts of interest in the research ethics literature has not translated into actual practice. Few institutions have policies regulating them and few institutional review boards (IRBs) take them into account. This suggests we need to go beyond mere discussion and identify ways to address these conflicts in practice.

For this purpose, existing guidance is limited in two ways. First, guidance on conflicts of interest generally focuses on researchers' financial conflicts. Second, the guidance that does exist on inherent conflicts tends to focus on clinician-investigators who are also the patient's treating clinician (Morain et al. 2019; Shah et al. 2015). Much less is available for research conducted by clinician-investigators who are distinct from the participants' own treating clinicians.

The lack of guidance is especially troubling given that standard practice is for researchers to discuss their studies with potential participants and then obtain their informed consent. This makes sense: The clinician-investigators know their studies better than others. In addition, they are also the ones who perform the clinical and research procedures included in the study, making it important for them to ensure that the participants give valid consent. At the same time, if potential participants do not enroll, researchers cannot obtain research data. The potential for this interest to affect how clinician-investigators describe the research, both prior to and as part of the consent process, underscores the need for guidance that will be adopted in practice.

One option would be to train researchers to recognize these inherent conflicts of interest and to understand that participants' interests always take precedence over collecting data. This seems reasonable, and an education program for researchers should be part of any overall approach. At the same time, clinician-investigators may be unaware of the ways in which their interest in collecting research data influences their recommendations to potential study participants. This suggests education will not be enough to protect participants.

Education of researchers could be supplemented with mandated disclosures in consent forms describing researchers' inherent conflict of interest (Sollitto et al. 2003). While disclosure is a widely endorsed response to conflicts of interest in general, it is unclear how useful it might be in the present case. Disclosing that clinician-investigators' interest in conducting the research might affect their description of the study does not put potential participants in a position to evaluate whether in fact it has done so.

Currently, IRBs review and approve the language included in research consent forms. This suggests that the greatest potential for inherent conflicts of interest to influence the information provided to participants comes during the discussions that occur prior to and as part of the consent process. One response would be to have someone other than the researchers discuss the study with potential participants and obtain their consent. This approach has the benefit of reducing the chances that the information provided to potential participants is inappropriately influenced by researchers' inherent conflict of interest. However, researchers typically understand their studies better than others, raising concern that this approach may lead to the information being inappropriately influenced by impoverished disclosure and discussion instead.

Relying on clinician-investigators alone to explain their research to potential participants seems inadequate. However, replacing the clinician-investigators with an independent party may undermine the disclosure. This also undermines the extent to which clinician-investigators are able to ensure that potential participants provide valid consent. These challenges suggest that a better option might be to have researchers discuss the study and obtain consent, with an independent party providing oversight. There are several options here.

An independent consultant might be tasked with reviewing the potential participant's history and medical record and evaluating the extent to which the research is in their clinical interest. Alternatively, an independent monitor might observe the discussions and consent process to ensure that the information is accurate and the participant understands it. Which of these or other approaches might be best will vary depending on the nature of the research and the potential participants' circumstances. This suggests that, rather than adopting a uniform approach for all studies, it might be better to determine on a case-by-case basis whether independent assessment is needed and, when it is, which approach would be best.

Of course, this is just one more recommendation that may have no influence on actual practice. To address this concern, IRBs might be charged with conducting these assessments, considering for each study they review whether the researchers' inherent conflicts of interest raise significant risk or concern.

When they do, the IRB should determine what safeguards are needed.

One might object that IRBs are already burdened with many tasks and we should avoid adding extra ones. However, IRBs are charged with ensuring that the research they approve is ethically appropriate. This includes protecting participants from potential harms posed by investigators' inherent conflicts of interest and determining whether these are being managed appropriately. The present proposal thus does not represent an expansion of IRB duties. It offers a way to help ensure that IRBs meet their existing obligations.

The potential conflict between collecting data as part of research and promoting participants' interests is inherent to clinical research. The research ethics literature highlights the extent to which it may undermine research participants' interests. However, there have been few efforts to address this concern in practice. To address this gap, we have argued that IRBs should assess this concern for each study they review. For many studies, the status quo of relying on clinician-investigators to discuss the study with potential participants and obtain their consent will be sufficient. This might be supplemented with education of investigators. For studies that raise greater concern, greater safeguards are needed. In these cases, the IRB can mandate additional protections, such as determination by an independent clinician of the extent to which participation is in participants' clinical interests and/or monitoring of the discussion and consent process.

DISCLOSURE STATEMENT

No potential conflict of interest was reported by the author(s).

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THE AMERICAN JOURNAL OF BIOETHICS
2020, VOL. 20, NO. 10, 96–98
https://doi.org/10.1080/15265161.2020.1806378

CASE COMMENTARIES

A Therapeutic Conundrum: Should a Physician Serve Simultaneously as Caregiver and Researcher?

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Physicians who place themselves simultaneously in the dual roles of serving as a patient's caregiver and as a clinical investigator with interest in enrolling that patient as a participant in clinical research face notable ethical challenges. This 70-year- old woman with advanced cancer undoubtedly is struggling with a decision on whether to undergo a risky surgery and is now confronted with medical advice much different

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