

## DATA, POLICIES AND CONFLICTS OF INTEREST IN RESEARCH

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### I. INTRODUCTION

In the wake of the death of Jesse Gelsinger in a gene transfer experiment at the University of Pennsylvania, substantial attention has focused on financial conflicts of interests (COIs) in research.<sup>1</sup> Numerous groups have promulgated policies and guidance regarding these COIs, which typically involve a series of procedural steps to assess and manage financial interests in research.<sup>2</sup> While a review of such policies is beyond the scope of this paper, they tend to share a common feature of considering disclosing financial interests to potential research participants. However, at the time many policies were crafted, little was known or specified about the process of disclosure, including who should disclose, what should be disclosed, when it should be disclosed, where it should be disclosed, how it should be disclosed, and what effects disclosure might have on the potential research participant and the research enterprise. For example, would disclosure affect willingness to participate in research? Would it affect trust? Nevertheless, the answers to such questions seem critical to understanding how such policies might be implemented, their potential effects, and their utility. The Conflict of Interest Notification Study (COINS) set out to provide systematic data about these and related issues.

COINS was a multi-year project funded by the National Institutes of Health and included a multidisciplinary team of scholars based at Duke University, Johns Hopkins University, and Wake Forest University.<sup>3</sup> At each stage of the project, COINS consulted an advisory panel, which consisted of individuals with expertise in clinical trials, conflicts of interest, ethics, and the

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1. See Robert Fretwell Wilson, *The Death of Jesse Gelsinger: New Evidence of the Influence of Money and Prestige in Human Research*, 36 AM. J.L. & MED. 295, 295-96 (2010).

2. See *id.* at 322.

3. Press Release, Johns Hopkins Medicine, *Disclosing Financial Conflicts of Interest to Research Participants May Not Be Enough* (Aug. 26, 2009), available at [http://www.hopkinsmedicine.org/news/media/releases/Disclosing\\_Financial\\_Conflicts\\_of\\_Interest\\_to\\_Research\\_Participants\\_May\\_Not\\_Be\\_Enough](http://www.hopkinsmedicine.org/news/media/releases/Disclosing_Financial_Conflicts_of_Interest_to_Research_Participants_May_Not_Be_Enough).

law; the panel had representatives from academia and industry.<sup>4</sup> In this paper, I review briefly what we learned over the course of the project and then discuss some barriers for gathering data about COIs that would enhance current understanding about these issues.

## II. WHAT WE LEARNED

COINS had several stages: 1) reviewing COI of policies; 2) obtaining stakeholder input; 3) developing model disclosure language and measures of trust; 4) evaluating the effects of disclosure; 5) considering the goals of disclosure; and 6) assessing COI management. I will discuss each of these in turn.

### A. COI Policies

At the time of our review, the policies of nearly half of academic medical centers in the United States that had an Institutional Review Board (IRB) mentioned the possibility of disclosing financial conflicts of interest to potential research participants.<sup>5</sup> In addition, more than half of those that mentioned disclosure included specific language that could be used.<sup>6</sup> However, there was substantial variability concerning the content of such disclosures.<sup>7</sup>

We subsequently compared the results of our policy review with the findings from interviews with IRB and Conflict of Interest Committee (COIC) officials (described below).<sup>8</sup> The interviews revealed a range of practices regarding the management of COIs that was broader than those suggested in written policies.<sup>9</sup> Further, COI and IRB officials interpreted and understood policies regarding COI differently.<sup>10</sup>

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4. Kevin P. Weinfurt et al., *Developing Model Language for Disclosing Financial Interests to Potential Clinical Research Participants*, IRB: ETHICS & HUMAN RES., Jan.-Feb. 2007, at 1, 2 [hereinafter Weinfurt et al., *Developing Model Language*].

5. Kevin P. Weinfurt et al., *Policies of Academic Medical Centers for Disclosing Financial Conflicts of Interest to Potential Research Participants*, 81 ACAD. MED. 113, 114 (2006).

6. *Id.*

7. *Id.* at 115.

8. Michaela A. Dinan et al., *Comparison of Conflict of Interest Policies and Reported Practices in Academic Medical Centers in the United States*, 13 ACCOUNTABILITY RES. 325, 328 (2006).

9. *Id.* at 333 tbl.4.

10. *Id.* at 340.

### B. Stakeholder Input

Given their relevant interests in COIs in research, we sought data from three stakeholder groups: 1) potential research participants; 2) institutional officials and investigators; and 3) study coordinators.

First, we conducted a series of focus groups with potential research subjects.<sup>11</sup> In these focus groups “we found that many participants want to know about financial interests in research, whether or not they report that such knowledge would affect their decision to participate. However, we documented great variability in participants’ desire and aptitude to understand the nature and implications of financial interests in clinical research.”<sup>12</sup> In addition, in contrast to most commentators on COI, some participants thought that financial interests in research might be beneficial.<sup>13</sup>

Second, we conducted interviews with selected IRB and COIC officials and investigators from academic medical centers, independent hospitals, and non-affiliated research entities.<sup>14</sup> The interviewees revealed a variety of approaches to disclosing financial interests in research as well as differing views on what is appropriate in this regard.<sup>15</sup>

Third, we surveyed study coordinators who are often charged with actually disclosing financial interests to potential research participants.<sup>16</sup> Based on the results, we concluded “that making information about financial interests in research readily available to clinical research coordinators, as well as providing education and training, would facilitate the disclosure of financial interests to potential research participants during the informed consent process.”<sup>17</sup>

### C. Model Disclosure Language and Measuring Trust

Using a multi-staged process, we developed model disclosure language that might be used to describe a variety of financial interests to potential research participants.<sup>18</sup> In crafting this language, we relied upon existing

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11. Kevin P. Weinfurt et al., *Views of Potential Research Participants on Financial Conflicts of Interest: Barriers and Opportunities for Effective Disclosure*, 21 J. GEN. INTERNAL MED. 901, 901 (2006).

12. *Id.* at 904.

13. *Id.* at 903.

14. Kevin P. Weinfurt et al., *Disclosing Conflicts of Interest in Clinical Research: Views of Institutional Review Boards, Conflict of Interest Committees, and Investigators*, 34 J.L. MED. & ETHICS 581, 582 (2006) [hereinafter Weinfurt et al., *Disclosing Conflicts of Interest*].

15. *Id.* at 583, 584 tbl.1.

16. Joëlle Y. Friedman et al., *Perspectives of Clinical Research Coordinators on Disclosing Financial Conflicts of Interest to Potential Research Participants*, 4 CLINICAL TRIALS 272, 273 (2007).

17. *Id.* at 278.

18. Weinfurt et al., *Developing Model Language*, *supra* note 4, at 3.

literature, expert review, reactions to draft language during focus groups with potential research participants, and cognitive pre-testing with potential research participants.<sup>19</sup>

As mentioned above, based on the uncertainties that disclosure of financial interests in research might have on trust, we wanted to be able to accurately measure this important outcome. Since there was no readily available measure of trust in medical researchers, we developed and tested appropriate scales.<sup>20</sup>

#### D. *Effects of Disclosure*

Using the empirically-derived model language, we tested the effects of disclosure in two separate studies. The first involved an internet-based survey of patients with asthma or diabetes.<sup>21</sup> Participants were given a description of a hypothetical study of a drug aimed at improving their disease.<sup>22</sup> All of the information about the studies was identical, except that participants were randomly assigned to one of five types of financial interest disclosures.<sup>23</sup> In most cases, financial interests had no significant differences on willingness to participate in the research and trust.<sup>24</sup> However, “[r]espondents consistently viewed a researcher owning equity less favorably than a researcher receiving per capita payments.”<sup>25</sup>

Although the internet-based study provided powerful data because of its size, it did not have great verisimilitude to actual clinical research practices. Therefore, we conducted a phone-based study involving cardiology patients.<sup>26</sup> In this study, patients received a letter from their cardiologist asking if they would be willing to participate in our survey.<sup>27</sup> Interested patients contacted our research team and were then sent a consent document for a hypothetical study involving a medication to improve cardiac disease.<sup>28</sup> Similar to the internet study, all information about the

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19. *Id.* at 2 tbl.1.

20. See Mark A. Hall et al., *Measuring Trust in Medical Researchers*, 44 *MED. CARE* 1048, 1050-51 (2006).

21. Kevin P. Weinfurt et al., *Effects of Disclosing Financial Interests on Attitudes Toward Clinical Research*, 23 *J. GEN. INTERNAL MED.* 860, 860-61, 865 (2008) [hereinafter Weinfurt et al., *Effects of Disclosing on Attitudes*].

22. *Id.* at 861.

23. *Id.*

24. *Id.* at 862, 865.

25. *Id.* at 863.

26. Kevin P. Weinfurt et al., *Effects of Disclosing Financial Interests on Participation in Medical Research: A Randomized Vignette Trial*, 156 *AM. HEART J.* 689, 689 (2008) [hereinafter Weinfurt et al., *Effects of Disclosing on Participation*].

27. *Id.*

28. *Id.*

hypothetical study was the same except that participants were randomly assigned to one of three disclosure conditions (per capita payments, equity interest, or no disclosure).<sup>29</sup> After the patient had received the material, the research assistant would review the consent document with them over the phone and ask about their willingness to participate in the hypothetical trial and measure trust.<sup>30</sup> The results were remarkably consistent with those of the internet study.<sup>31</sup>

#### E. Goals of Disclosure

In aggregate, the data we accumulated suggested that there was a lack of clarity about the goals of disclosing financial interests in research and that there can be barriers to meeting them. Such goals include: promoting informed decision making; respecting participants' perceived right to know; establishing or maintaining trust; minimizing risk of legal liability; deterring troubling financial relationships; and protecting participants' welfare.<sup>32</sup> In the end, disclosure alone seems to be an incomplete management tool for financial interests in research.<sup>33</sup> Rather, it is best considered an important component of management strategies.

#### F. COI Management

Given the importance of management strategies, COINS conducted some preliminary research to begin to describe some of the structural issues that may be relevant to COIs and the management approaches being used in different settings. Based on a small number of interviews with staff at health care organizations across the nation, it became apparent that the way investigators are compensated in clinical research settings outside of academic medical centers, such as community hospitals, may affect whether financial interests indeed pose a conflict.<sup>34</sup> In addition, a variety of different methods are used to address financial interests in research. A survey of institutions that participate in high-profile clinical research confirmed that different approaches to oversight are used.<sup>35</sup> Finally, since per capita

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29. *Id.* at 690.

30. *Id.*

31. Compare Weinfurt et al., *Effects of Disclosing on Participation*, *supra* note 26, at 691, with Weinfurt et al., *Effects of Disclosing on Attitudes*, *supra* note 21, at 862.

32. Kevin P. Weinfurt et al., *Disclosure of Financial Relationships to Participants in Clinical Research*, 361 *NEW ENG. J. MED.* 916, 917 tbl.1 (2009).

33. See *id.* at 920.

34. Mark A. Hall et al., *Community Hospital Oversight of Clinical Investigators' Financial Relationships*, *IRB: ETHICS & HUMAN RES.*, Jan.-Feb. 2009, at 9-10.

35. Kevin P. Weinfurt et al., *Oversight of Financial Conflicts of Interest in Commercially Sponsored Research in Academic and Nonacademic Settings*, 25 *J. GEN. INTERNAL MED.* 460, 463 (2010).

payments in clinical research are commonplace, we explored some of the issues related to assessing the acceptability of particular payments. Clearly, more attention should focus on how per capita payments for research are determined and used in order to assess more accurately whether they pose a COI.<sup>36</sup>

### III. BARRIERS TO GATHERING DATA ABOUT COIS

While the COINS team was able to gather systematic data concerning the disclosure of financial interests to potential research participants, barriers were encountered with respect to two important related areas: nesting a study of different disclosures in the context of actual clinical research and assessing non-financial conflicts of interest.

#### A. *Nesting a Study in an Actual Clinical Trial*

As COINS was being developed, we envisioned conducting a randomized study of different approaches to disclosing financial interests in the context of an actual clinical trial. This method would be best suited to provide strong evidence regarding whether the empirically developed disclosure language in COINS performed better than existing language. While we had substantial experience nesting trials related to informed consent in actual research settings,<sup>37</sup> the proposed study proved to be especially challenging for a variety of reasons. First, in order to conduct a nested study about the disclosure of financial interests in research, we needed to identify a large enough study to have statistical power to compare different approaches to disclosure. Realistically, this required identifying a trial being conducted at several institutions. However, because individual IRBs and COICs may use different templates for disclosure,<sup>38</sup> it would be difficult to make a meaningful comparison. Moreover, the necessity for multiple reviews would likely undermine our ability to field the trial. A practical and ethically acceptable alternative was to identify a multi-institutional study that was being overseen by an independent IRB that also manages financial interests in research. As it turns out, following a meeting with its members, a prominent independent IRB was willing to collaborate on a trial, testing its standard disclosure language against the COINS empirically derived language. Next, we had to identify a trial in which actual financial interests were in play, necessitating that we identify an industry-sponsored trial. Accordingly, we discussed the possibility of collaborating

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36. Mark A. Hall et al., *Per Capita Payments in Clinical Trials: Reasonable Costs Versus Bounty Hunting*, 85 ACAD. MED. 1554, 1554-56 (2010).

37. See, e.g., Philip W. Lavori et al., *Quality Assurance Questionnaire for Professionals Fails to Improve the Quality of Informed Consent*, 4 CLINICAL TRIALS 638, 638-39 (2007).

38. Weinfurt et al., *Disclosing Conflicts of Interest*, *supra* note 14, at 582, 584 tbl.1.

with several different sponsors. Although there was substantial interest in the research question, ultimately industry sponsors elected not to collaborate, tending to cite their corporate fiduciary obligations. Simply put, even though financial interests are part of their work, drawing attention to the issue of COI was seen to be risky. Thus, without willing collaborators, we had to abandon the possibility of testing alternative disclosure language in the context of actual research, relying instead on the hypothetical approaches described earlier.

#### B. *Non-Financial Conflicts of Interest*

Although substantial attention has focused on financial COIs, anecdotal evidence suggests that non-financial conflicts may pose substantial risks to the integrity of the research enterprise. For instance, James Wilson, who was the principal investigator in the trial in which Jesse Gelsinger was enrolled, describes such conflicts.<sup>39</sup> However, given the lack of systematic data regarding the nature of non-financial and their potential relationship to research integrity and safety, a subset of the COINS team and others set out to explore this issue. In crafting the proposal, the team recognized that unlike financial interests that are easily quantified, non-financial conflicts would likely be difficult to define and understand. Accordingly, the proposal included the use of qualitative methods at the outset, such as using focus groups and key-informant interviews, to help develop an online survey. Unfortunately, the proposal for this work was not funded. Perhaps this was related to the difficulty that can be encountered in getting qualitative research funded or that the topic itself was threatening.<sup>40</sup> Regardless, this important work remains undone.

#### IV. CONCLUDING COMMENTS

Despite the barriers encountered in obtaining some information about COIs in research, it has been possible to build a rich data set concerning the disclosure of financial interests to potential research participants. These data are well situated to enhance disclosure through informed policies and practices. In addition, these data challenge some of our assumptions and conceptual understandings about financial interests in research. Future research should be directed at examining and testing management strategies for financial interests in research as well as exploring systematically the nature of non-financial COIs in research.

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39. James M. Wilson, *Lessons Learned from the Gene Therapy Trial for Ornithine Transcarbamylase Deficiency*, 96 *MOLECULAR GENETICS & METABOLISM* 151, 152, 156 (2009).

40. Martha Ann Carey & Janice Swanson, *Funding for Qualitative Research*, 13 *QUALITATIVE HEALTH RES.* 852, 852 (2003).

