RESEARCH ETHICS

Potential research participants’ views regarding researcher and institutional financial conflicts of interest

S Y H Kim, R W Millard, P Nisbet, C Cox, E D Caine

Background: Financial conflict of interest in clinical research is an area of active debate. While data exist on the perspectives and roles of academic institutions, investigators, industry sponsors, and scientific journals, little is known about the perspectives of potential research participants.

Methods: The authors surveyed potential research participants over the internet, using the Harris Interactive Chronic Illness Database. A potential research participant was defined by: (1) self report of diagnosis by a health care professional and (2) willingness to participate in clinical trials. Email invitations were sent to 20,205 persons with coronary artery disease, breast cancer, or depression; a total of 6363 persons were screened; of these, 86% or 5478 met inclusion criteria and completed the survey. The outcome measures were respondents’ ratings on: importance of knowing conflict of interest information, whether its disclosure ought to be required, and its effect on willingness to participate—across seven widely discussed scenarios of financial conflicts of interest (ranging from commercial funding to equity ownership).

Results: Majority responded that knowing conflict of interest information was “extremely” or “very” important; a larger majority felt financial conflicts of interest should be disclosed as part of informed consent (64% to 87%). In all seven scenarios, a majority was still willing to participate but in some scenarios a sizable minority would be wary of participation. Respondents were more wary of individual than institutional conflicts of interest. Illness group and sociodemographic factors had modest effects and did not affect the main trends.

Conclusions: The prevailing practice of non-disclosure of financial conflicts of interest in clinical research appears contrary to the values of potential research participants.
and were screened. Of these, 5478 or 86% stated their willingness to participate in a clinical trial at the time of the survey and were asked to complete the full survey. A sweepstakes incentive was used so that three respondents won $500 each for completing the survey.

Survey instrument

By sending large numbers of email invitations, it was possible for thousands of respondents to simultaneously complete the survey online. Advanced survey techniques were used to adapt the survey instrument to the online environment, including password protection, programmed skip patterns, visually appealing fonts and formatting, random rotations of questions, range checks, and consistency checks. These checks were employed as the data were tabulated.

The instrument did not mention the phrase “conflict of interest” although seven conflict of interest scenarios were presented. All the scenarios considered a new drug for treatment of the respective illnesses of the respondents. The conflict of interest scenarios used were those widely discussed in the literature: commercial funding of clinical trials,19 personal income earned by investigators from the manufacturer of the new medication being tested,7 per capita enrolment payment to investigators,20 investigator and university ownership of patents for the medication being tested,11 investigator or university ownership of stocks in the company whose product is being tested,24 and investigator or university ownership of stocks in the company. The value of the company’s stocks can rapidly go up or down by large amounts depending on whether the drug is seen to be safe and effective for treating [respondent’s illness].

The survey questions were reviewed by experts (an IRB executive director, a senior medical centre official responsible for human subjects’ research integrity, and a bioethicist with experience in drafting conflict of interest policies for a major medical association) and pretested with 10 lay persons in print form. The electronic version was pretested and revised by three of the authors (SYHK, PN, and RM) in collaboration with survey quality assurance team at Harris Interactive Inc.

Data analysis

Since the survey questions involved ordered, categorical responses, the effects of scenario and illness group on responses were analysed using a two way repeated measures analysis of variance modified for ordinal data,27 Illness group was the between subjects factor and scenario was a within subjects factor. Each analysis of variance was run using the levels indicated in table 3.

RESULTS

The characteristics of the survey completers and of those in the Chronic Illness Database for each illness group are described in table 3.
A summary tabulation of the responses to each survey question for each scenario is given in table 4.

What effect might such conflict of interest information have on the potential research participants? In all scenarios, a minority stated they would be less inclined (range 3% to 44%) to participate or said they would in fact not participate (range 2% to 32%) in a clinical trial because of the conflicts of interest information given in the scenarios. Thus a majority would still consider participating in studies with researcher and institutional financial conflicts of interest. Indeed, for the commercial funding scenario, being told that a drug company is funding the study would make a large minority (41% to 46%) more inclined to participate than if such information had not been disclosed to them.

For the personal income scenario, only a small portion of respondents used the amount of money received by the researcher as a deciding factor in answering their questions (range 7–14%). Of those respondents, 64–78% would require informed consent, or be disinclined to participate, or not participate when the line was drawn at greater than $10 000 (an often mentioned threshold). For example, 10% of respondents with depression answered that whether researchers should be required to disclose personal income from the drug manufacturer should depend on the amount of personal income. If the threshold is set at “greater than $10 000”, 78% of those 10% would require informed consent.

We further examined the summary descriptive data through multivariate analysis. The results of the repeated measures two-way analysis of variance showed that a scenario effect was present in responses to all four questions. This is summarised in table 5 as rankings of the scenarios in terms of their effects on responses.

An index of overall rankings was created using a simple average rank score for each scenario. The results were:
Table 4  Percentage of responses in each response category to the four survey questions, for each conflict of interest scenario, of each illness group

<table>
<thead>
<tr>
<th></th>
<th>Commercial funding</th>
<th>Personal income*</th>
<th>Per capita payment</th>
<th>Researcher patent</th>
<th>University patent</th>
<th>Researcher stocks</th>
<th>University stocks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H  B  D</td>
<td>H  B  D</td>
<td>H  B  D</td>
<td>H  B  D</td>
<td>H  B  D</td>
<td>H  B  D</td>
<td>H  B  D</td>
</tr>
<tr>
<td>Importance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extremely/very</td>
<td>56  62  51</td>
<td>58  69  56</td>
<td>50  61  46</td>
<td>59  64  59</td>
<td>56  65  57</td>
<td>66  72  65</td>
<td>64  69  62</td>
</tr>
<tr>
<td>Somewhat</td>
<td>27  26  31</td>
<td>24  19  26</td>
<td>27  23  26</td>
<td>21  21  21</td>
<td>24  22  24</td>
<td>17  15  19</td>
<td>19  18  21</td>
</tr>
<tr>
<td>Not very/at all</td>
<td>17  12  19</td>
<td>17  12  18</td>
<td>23  16  28</td>
<td>20  15  20</td>
<td>20  14  20</td>
<td>17  13  17</td>
<td>17  13  18</td>
</tr>
<tr>
<td>IC requirement†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>81  87  78</td>
<td>68  74  64</td>
<td>70  78  64</td>
<td>76  82  75</td>
<td>76  82  74</td>
<td>80  85  78</td>
<td>79  84  76</td>
</tr>
<tr>
<td>Yes, depends on amount</td>
<td>–  –  –</td>
<td>7  9  10</td>
<td>–  –  –</td>
<td>–  –  –</td>
<td>–  –  –</td>
<td>–  –  –</td>
<td>–  –  –</td>
</tr>
<tr>
<td>Inclination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More</td>
<td>46  42  41</td>
<td>16  10  11</td>
<td>17  12  13</td>
<td>12  11  9</td>
<td>16  16  15</td>
<td>8  5  6</td>
<td>8  6  7</td>
</tr>
<tr>
<td>Same as before</td>
<td>50  52  53</td>
<td>53  46  50</td>
<td>68  65  70</td>
<td>62  67  60</td>
<td>72  75  70</td>
<td>55  59  54</td>
<td>66  69  65</td>
</tr>
<tr>
<td>Less</td>
<td>3  6  6</td>
<td>22  31  28</td>
<td>16  23  17</td>
<td>26  23  31</td>
<td>12  10  15</td>
<td>37  36  40</td>
<td>26  24  28</td>
</tr>
<tr>
<td>Less, depends on amount</td>
<td>–  –  –</td>
<td>8  13  11</td>
<td>–  –  –</td>
<td>–  –  –</td>
<td>–  –  –</td>
<td>–  –  –</td>
<td>–  –  –</td>
</tr>
<tr>
<td>Behaviour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Still consider</td>
<td>89  82  86</td>
<td>79  67  70</td>
<td>83  74  80</td>
<td>75  72  68</td>
<td>86  84  80</td>
<td>65  61  59</td>
<td>71  68  66</td>
</tr>
<tr>
<td>Unsure</td>
<td>9  16  12</td>
<td>10  15  11</td>
<td>12  17  14</td>
<td>8  11  11</td>
<td>18  26  21</td>
<td>17  23  20</td>
<td></td>
</tr>
<tr>
<td>Not participate</td>
<td>2  3  3</td>
<td>12  18  18</td>
<td>7  11  9</td>
<td>13  11  17</td>
<td>5  5  9</td>
<td>17  14  20</td>
<td>12  10  14</td>
</tr>
<tr>
<td>Not participate, depends on amount</td>
<td>–  –  –</td>
<td>9  14  12</td>
<td>–  –  –</td>
<td>–  –  –</td>
<td>–  –  –</td>
<td>–  –  –</td>
<td>–  –  –</td>
</tr>
</tbody>
</table>

H indicates heart disease group (n = 2355), B indicates breast cancer group (n = 1006), and D indicates depression group (n = 2117).

*For the personal income scenario only, the respondents were given an extra response option for the informed consent requirement, inclination, and behaviour questions to assess whether the amount of personal income received by the researcher was a determining factor. The amount categories were: greater than $100, greater than $1000, greater than $5000, greater than $10 000, greater than $50 000. For the behaviour question in this scenario, “unsure” response was not an option.

†IC indicates informed consent. The majority of respondents felt that financial arrangement information contained in all seven scenarios was extremely or very important. For all scenarios, a clear majority (range 64% to 87%) responded that researchers should be required to disclose the financial arrangements.
The effect of the conflict of interest scenario and of belonging to one of three illness groups on survey responses, summarised as a ranking of the seven scenarios for each illness group for each survey question.

Table 5

<table>
<thead>
<tr>
<th>Rank</th>
<th>Researcher stocks</th>
<th>University stocks</th>
<th>Commercial funding</th>
<th>Per capita fee</th>
<th>Personal income</th>
<th>Per capita fee</th>
<th>University patent</th>
<th>Personal income</th>
<th>Per capita fee</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Researcher stocks</td>
<td>University stocks</td>
<td>Commercial funding</td>
<td>Per capita fee</td>
<td>Personal income</td>
<td>Per capita fee</td>
<td>University patent</td>
<td>Personal income</td>
<td>Per capita fee</td>
</tr>
<tr>
<td>2</td>
<td>University stocks</td>
<td>Researcher stocks</td>
<td>Commercial funding</td>
<td>Per capita fee</td>
<td>Personal income</td>
<td>Per capita fee</td>
<td>University patent</td>
<td>Personal income</td>
<td>Per capita fee</td>
</tr>
<tr>
<td>3</td>
<td>Researcher stocks</td>
<td>University stocks</td>
<td>Commercial funding</td>
<td>Per capita fee</td>
<td>Personal income</td>
<td>Per capita fee</td>
<td>University patent</td>
<td>Personal income</td>
<td>Per capita fee</td>
</tr>
<tr>
<td>4</td>
<td>University stocks</td>
<td>Researcher stocks</td>
<td>Commercial funding</td>
<td>Per capita fee</td>
<td>Personal income</td>
<td>Per capita fee</td>
<td>University patent</td>
<td>Personal income</td>
<td>Per capita fee</td>
</tr>
<tr>
<td>5</td>
<td>Researcher stocks</td>
<td>University stocks</td>
<td>Commercial funding</td>
<td>Per capita fee</td>
<td>Personal income</td>
<td>Per capita fee</td>
<td>University patent</td>
<td>Personal income</td>
<td>Per capita fee</td>
</tr>
<tr>
<td>6</td>
<td>University stocks</td>
<td>Researcher stocks</td>
<td>Commercial funding</td>
<td>Per capita fee</td>
<td>Personal income</td>
<td>Per capita fee</td>
<td>University patent</td>
<td>Personal income</td>
<td>Per capita fee</td>
</tr>
<tr>
<td>7</td>
<td>University stocks</td>
<td>Researcher stocks</td>
<td>Commercial funding</td>
<td>Per capita fee</td>
<td>Personal income</td>
<td>Per capita fee</td>
<td>University patent</td>
<td>Personal income</td>
<td>Per capita fee</td>
</tr>
</tbody>
</table>

1. Higher the ranking more likely a scenario is to elicit the responses of greater importance, higher rate of answering less inclined to participate, and higher rate of answering would not participate based on the conflict of interest scenario contained in that scenario. The four scenarios with highest average ranking are flagged by the symbols *, †, ‡, and $ in table 5. Thus, with the exception of the university stock ownership scenario, the three scenarios depicting personal financial incentives for the individual researcher tended to elicit the highest importance and greatest negative (that is, feel disinclined to participate, or would not participate) responses.

2. The results of the informed consent requirement question showed no interaction between scenario and illness so that the rankings are given for the three illness groups combined.

3. Scenarios labelled with same superscript numbers show no significant pairwise scenario differences (p < 0.0001) or level. There were significant interaction effects between scenario and illness for all except the informed consent question, as can be seen from the variations in rankings of the scenario effects depending on the illness group.

DISCUSSION

While the perspective of research subjects is becoming an increasing focus of research, little is known about their attitudes and potential behavioural responses to researcher and institutional conflicts of interest. Aside from one anecdotal account by an industry executive, we found one survey of 200 medical outpatients regarding their attitudes toward financial incentives of doctors in Phase IV post-marketing research whose findings are generally consistent with our results. Our study examined a wider variety of scenarios and, more importantly, surveyed people who actually had illnesses of interest and were interested in participating in research. Further, we measured not only attitudes but also potential behavioural consequences of disclosing conflict of interest information.

Implications of study findings

The main, robust finding of our study is a dual trend: (1) most potential research participants desire to be informed (and believe this should be required) regarding financial conflicts of information in research even while (2) still wanting to participate in such research. The potential research participants’ desire and demand to know such information is unlikely to be based upon a pre-existing distrust of research: this group consisted of only those already willing to participate in research. Indeed, a clear majority would still consider participating in clinical trials with even the most controversial conflict of interest present (researcher’s substantial equity interest in the company whose product is being studied). Instead, in our study the potential research participants’ responses echo past studies on patient preferences for autonomy in medical decision making. Those studies found that patients value being informed even if they are willing to defer decisions to their physicians.

Thus the presumption by some that a disclosure of financial arrangements by its very existence casts suspicion on the party with the conflict of interest was not borne out. In an unexpected finding, nearly half of the respondents said they were more inclined to participate in a clinical trial if they knew that “the drug company whose product is being studied...
is funding the study.” While the analysis of the open ended comments provided by our respondents is not yet complete, a common answer among those more inclined to participate was the respondent’s desire to assess the company’s reputation. As one respondent put it, “I would feel better about it if it was a well known company funding the project.”

However, a sizable minority would not participate in research that has certain conflicts of interest present. Namely, if the researcher owns substantial equity stake in the sponsoring company or if the researcher earns personal income from the sponsor. (It is interesting to note that while the current federal regulations and, consequently, policy debates emphasise amount thresholds, only a small minority of our respondents conditioned their responses upon the amounts involved.)

Given these findings, it is difficult to defend the practice of non-disclosure: if one knows that a sizable number, were they informed, would not wish to participate, then it may be unethical not to inform them of those facts in the absence of strong countervailing reasons.16

The presence of significant scenario effects is an important finding. The pattern of responses suggests that the respondents were more wary of individual investigators’ conflicts of interest than of institutional ones. However, this does not mean that the respondents did not see institutional conflicts as a problem: the university stocks scenario ranked second in raising concerns from the respondents. Further, the most problematic conflict of interest situation—that is, an investigator owning substantial equity stake in a company whose product is being tested—evoked the greatest wariness from the respondents. This may simply confirm the fact that financial arrangement information is not technical, scientific detail that may confuse the potential research participants. A rationale sometimes cited against a policy of disclosure.14

Instead, such information may be comprehensible by most people and may form an important basis for expressing their values by agreeing or disagreeing to participate in some research. For instance, we found that most who say they would decline to participate, not unexpectedly cited potential for bias and concern about safety as their reasons. However, those who felt more inclined to participate gave coherent reasons as well. For instance, for the researcher patent ownership scenario, some focused on the presumed expertise of a patent owner (“I would be getting the benefit of first hand knowledge from the researcher.”)

Illness type and education had significant and consistent, if modest, effects on response patterns. These are findings that need further study and may have implications for designing contextually sensitive informed consent procedures. We note that although some sociodemographic and illness variables had statistically significant effects, the effect sizes were relatively small in comparison with the robust main trend of persons placing high value on the conflict of interest information and yet who were willing to participate in such research.

**Limitations**

There are limitations to this study. Firstly, it is inherently difficult to operationalise the concept of a “potential research participant” since all clinical trials rely on self selected patient volunteers. Despite this difficulty, given the important yet neglected ethical voice of such persons, we chose to use two necessary, but admittedly not exhaustive, criteria to define a potential research participant. To the extent that the self selection qualities of our sample recapitulate those of actual research participants, the results of this study convey the values of a population of legitimate stakeholders in the financial conflicts of interest debate.

Secondly, the overall response rate was relatively low. It should be noted, however, that the respondent group reflected the sociodemographic features of the entire database. Further, because of the large sample size, we were able to perform meaningful multivariate analyses to show that the main findings are quite robust, even after accounting for several potential confounding factors.

Finally, there are potential limitations in the use of the internet for survey research. Despite the precautions taken in our procedures, the “digital divide” might make the sample frame itself unrepresentative of potential research participants. Around the time of this survey, 56% to 59% of all Americans were on the internet.15 Thirty eight per cent of those earning under $30,000, 37% of those with high school education or less, 43% of blacks, and 47% of Hispanics were using the internet.16 The lower than expected number of minority respondents in this study reflects the lower than expected number of minorities in the Harris Interactive Chronic Illness Database and may reflect their unwillingness to be part of such a database. Because the use of the internet for research is relatively new, we do not yet know whether there is an uncorrectable bias due to the fact that Americans using the internet—especially those willing to be part of a health survey database—are fundamentally different from the non-users, in ways unaccounted for by education, income, sex, race/ethnicity, and age. We note again, however, that although our responding group was overwhelmingly white, the large number of respondents contained enough persons from a wide range of sociodemographic (including racial and ethnic) backgrounds to conduct meaningful multivariate analyses.

**CONCLUSIONS**

The current debate over financial conflicts of interest in clinical research focuses on institutional policies and on individual researchers’ conflicts of interest. It is unclear whether disclosure, management, or elimination of conflicts of interest is the best solution. Our study should not be taken to mean that only disclosure is required. It supports disclosure but it did not examine the further issues on management or elimination of conflict directly. It is probably wise to interpret the apparent willingness of potential research participants to tolerate substantial conflicts of interest to mean that it is not too late to make the financial aspects of clinical research more transparent to all.

This study provides a clear answer to the question of whether or not potential research participants want to know the financial conflicts of interest of researchers and institutions.17 They clearly and overwhelmingly do. Our respondents were also able to make distinctions between the different types of conflicts of interest. Financial conflict of interest is not a technical or complex concept understandable only by researchers and their institutions. Concern over financial conflicts of interest requires not so much an intimate knowledge about science as some intuitive grasp of ordinary human behaviour.

We cannot tell from this study whether the current high level of trust in researchers and their institutions will continue as more stories of alleged adverse outcomes related to financial conflicts of interest arise.18 However, it appears that the current practice of non-disclosure of worrisome conflicts of interest do not conform to the values and wishes of potential patient volunteers without whose participation no research can occur.

**ACKNOWLEDGEMENTS**

We thank Jason Karlawish, MD for a critical review of the manuscript, Cynthia Dunn, MD for critical review of the survey questionnaire and of the manuscript, and Gary Chadwick, PharmD...
and David Orentlicher, MD, JD for critical review of the survey questionnaire.

Authors’ affiliations
S Y H Kim, E D Caine, Department of Psychiatry, University of Rochester Medical Center, Rochester NY, USA
C Cox, Biometry and Mathematical Statistics Branch, National Institute of Child Health and Human Development, Bethesda MD, USA
R W Millard, P Nisbet, HarrisInteractive, Inc, Rochester, NY, USA

This study was in part supported by NIMH grant MH-18911, an American Association for Geriatric Psychiatry Eisai-Pfizer Alzheimer’s Disease Research Fellowship, and the Rivas Endowment of the Department of Psychiatry, University of Rochester.

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doi: 10.1136/jme.2002.001461

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