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 6,363 persons were screened; of these, 86% or 5,478 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, personal income earned by investigators from the manufacturer of the new medication being tested, per capita enrolment payment to investigators, investigator and university ownership of patents for the medication being tested, and investigator or university ownership of stocks in the company whose product is being tested.

The seven scenarios were presented in random order to the respondents. Each respondent answered only from the perspective of his or her own self reported chronic illness. The scenario descriptions and the questions used are given in tables 1 and 2.

The four survey questions fell into two domains: the value placed on knowing the conflict of interest information (importance question and informed consent requirement question) and the reactions to such information (inclination question and behaviour question). While the two questions in each domain are similar, we were interested in both a general question for each domain as well as obtaining responses to specific questions of policy interest.

The inclination and behaviour questions were each followed up with an open ended invitation to comment on their answers. A qualitative analysis of these responses is underway; selected responses are included below, for illustrative purposes.

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.

Table 1 Seven scenarios of financial conflicts of interest in clinical research

<table>
<thead>
<tr>
<th>Conflict type label</th>
<th>Scenario description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial funding</td>
<td>Imagine that even though the study will be done at a university medical centre, the company that makes the new drug is paying for the study.</td>
</tr>
<tr>
<td>Personal income</td>
<td>Imagine that the researcher conducting this study receives personal income from the study drug’s manufacturer, from activities such as consulting, being on advisory boards, and giving lectures at company sponsored events.</td>
</tr>
<tr>
<td>Per capita payments</td>
<td>Imagine that the drug company pays the researcher a lump sum of money per patient enrolled in the study that is greater than the expenses required to conduct the study. The money left after expenses goes into the researcher’s budget and is used in a variety of ways—for example, for other research projects, for travel to meetings, and for support staff, etc. at the discretion of the researcher.</td>
</tr>
<tr>
<td>Researcher patent</td>
<td>Suppose the researcher owns the patent on the drug being studied. If this drug is found to be safe and effective for treating [respondent’s illness], the researcher would receive a part of the profits from the sales of the drug.</td>
</tr>
<tr>
<td>University patent</td>
<td>Suppose the university medical centre owns the patent on the drug. If it is found to be safe and effective in treating [respondent’s illness], the university would receive a part of the profits from the sales of the drug.</td>
</tr>
<tr>
<td>Researcher stocks</td>
<td>Suppose the new drug is made by a small biotechnology company. The researcher owns a substantial portion of the stocks of 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].</td>
</tr>
<tr>
<td>University stocks</td>
<td>Suppose the drug is made by a small biotechnology company. The university medical centre owns substantial portion of the stocks of 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].</td>
</tr>
</tbody>
</table>

*Each respondent answered questions for all seven scenarios. The scenarios were presented in random order to each respondent and customised to each respondent’s self reported diagnosis.

RESULTS

The characteristics of the survey completers and of those in the Chronic Illness Database for each illness group are described in table 3.

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. Illness group was the between subjects factor and scenario was a within subjects factor. Each analysis of variance was run both with and without interactions; if the test for interaction was negative, the model without the interaction was used. Pairwise comparisons of scenario effects on the responses for each survey question were performed using a two tailed significance level of 0.01 chosen to account for multiple comparisons. For the informed consent requirement question, because no interaction occurred between scenario and illness, pair-wise scenario effect comparisons were not done separately for each illness group but with responses of all three groups combined. For each of the four survey questions, the seven scenarios were ranked according to their effects, for each illness group (again, except for the informed consent requirement question). By the convention used in this paper, higher rank of a scenario means that, in comparison with the other scenarios, it tended to elicit responses of: greater likelihood of attributing higher importance, greater likelihood of requiring informed consent, greater likelihood of being disinclined to participate, and greater likelihood of saying one would not participate based on the conflict of interest information. Finally, a simple average rank score for each scenario, as an estimate of its overall effect on the responses by those surveyed, was also calculated.

The influence of demographic variables of sex, age, education, income, race/ethnicity, as well as of illness category on the responses of our subjects were analysed using multinomial logistic regression, using the levels indicated 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>
<thead>
<tr>
<th>Label for type of question</th>
<th>Question and answer choices</th>
<th>Response options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Importance question</td>
<td>How important is it for you to know [the financial arrangement information] before you consent to be in this study?</td>
<td>Extremely important</td>
</tr>
<tr>
<td>Informed consent requirement question</td>
<td>Do you think that the researcher should be required to tell you [the financial arrangement information] before you are asked to participate?</td>
<td>Yes</td>
</tr>
<tr>
<td>Inclination question</td>
<td>Which option best reflects how you would feel about this study, given [the financial arrangement information]?</td>
<td>More inclined to participate</td>
</tr>
<tr>
<td>Behaviour question</td>
<td>Which option best reflects what you would do, given [the financial arrangement information]?</td>
<td>I would still consider participating in this study</td>
</tr>
</tbody>
</table>

Table 2 Questions answered by the respondents for each of the seven financial conflicts of interest scenarios

<table>
<thead>
<tr>
<th>Table 3 Characteristics of survey respondents and of persons in the Harris Interactive Chronic Illness Database, according to self reported diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat disease</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Women (%)</td>
</tr>
<tr>
<td>Age (%)</td>
</tr>
<tr>
<td>18–29</td>
</tr>
<tr>
<td>30–44</td>
</tr>
<tr>
<td>45–64</td>
</tr>
<tr>
<td>65+</td>
</tr>
<tr>
<td>Education (%)</td>
</tr>
<tr>
<td>High school or less</td>
</tr>
<tr>
<td>Some college</td>
</tr>
<tr>
<td>College</td>
</tr>
<tr>
<td>Post-college</td>
</tr>
<tr>
<td>Income (%)</td>
</tr>
<tr>
<td>$&lt;25K</td>
</tr>
<tr>
<td>25 to &lt;50</td>
</tr>
<tr>
<td>50K to &lt;100K</td>
</tr>
<tr>
<td>$&gt;100K</td>
</tr>
<tr>
<td>No answer</td>
</tr>
<tr>
<td>Race (%)</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Black/African</td>
</tr>
<tr>
<td>American</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

*Per cent of 45 to 60 year old persons.
†Per cent of persons over 60 years old.
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>Scenario</th>
<th>Per capita payment</th>
<th>Researcher patent</th>
<th>University patent</th>
<th>Commercial funding</th>
<th>Personal income</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBDHBDHBDHBDHBDHBDHBD</td>
<td>Extremely/very</td>
<td>56</td>
<td>62</td>
<td>51</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>Somewhat</td>
<td>27</td>
<td>26</td>
<td>31</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Not very/at all</td>
<td>17</td>
<td>12</td>
<td>19</td>
<td>17</td>
</tr>
</tbody>
</table>

IC requirement

- Yes | 81 | 87 | 78 | 68 | 74 | 64 | 70 | 78 | 64 | 76 | 82 | 75 | 75 | 82 | 74 | 80 | 85 | 78 | 79 | 84 | 76 |
- Yes, depends on amount | – | – | – | 7 | 9 | 10 | – | – | – | – | – | – | – | – | – | – | – | – | – | – |

Inclination

- More | 46 | 42 | 41 | 16 | 10 | 11 | 17 | 12 | 13 | 12 | 11 | 9 | 16 | 16 | 15 | 8 | 56 | 86 | 76 |
- Same as before | 50 | 52 | 53 | 53 | 46 | 50 | 68 | 65 | 70 | 62 | 67 | 60 | 72 | 75 | 70 | 55 | 59 | 54 | 58 | 65 |
- Less | 3 | 6 | 6 | 22 | 31 | 28 | 16 | 23 | 17 | 26 | 23 | 31 | 12 | 10 | 16 | 37 | 36 | 40 | 26 | 24 | 28 |
- Less, depends on amount | – | – | – | 8 | 13 | 10 | – | – | – | – | – | – | – | – | – | – | – | – | – | – |

Behaviour

- Still consider | 89 | 82 | 86 | 79 | 67 | 70 | 83 | 74 | 80 | 75 | 72 | 68 | 86 | 84 | 80 | 65 | 61 | 59 | 59 | 71 |
- Unsure | 9 | 16 | 12 | 10 | 15 | 11 | 12 | 17 | 14 | 8 | 11 | 11 | 18 | 26 | 21 | 23 | 20 |
- Not participate | 2 | 3 | 3 | 12 | 18 | 18 | 7 | 11 | 9 | 13 | 11 | 17 | 55 | 9 | 7 | 1 | 4 | 2 | 0 | 1 | 2 |
- Not participate, depends on amount | – | – | – | 9 | 14 | 12 | – | – | – | – | – | – | – | – | – | – | – | – | – | – |

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>
<thead>
<tr>
<th>Researcher stocks</th>
<th>University stocks</th>
<th>University stocks</th>
<th>University stocks</th>
<th>University stocks</th>
<th>University stocks</th>
<th>University stocks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart disease</td>
<td>Breast cancer</td>
<td>Depression</td>
<td>Heart disease</td>
<td>Breast cancer</td>
<td>Depression</td>
<td>Heart disease</td>
</tr>
<tr>
<td>Importance</td>
<td>Informed consent</td>
<td>Inclination</td>
<td>Behaviour</td>
<td>Heart disease</td>
<td>Breast cancer</td>
<td>Depression</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

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" was a financial benefactor. Instead, in our study the majority would still consider participating in clinical trials with even the most controversial conflict of interest present. However, the potential research participants’ desire and demand to know such information is unlikely to be based on 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 regulations2 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 bias and concern about safety as their reasons. However, those who felt more inclined to participate gave coherent strong countervailing reasons. 18 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 the best solution. Our study should not be taken to mean that it is not too late to make the financial disclosure but it did not examine the further issues on management or elimination of conflicts of interest 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.7 They clearly and overwhelming do. Our respondents were 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.24 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.

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. They clearly and overwhelmingly do. Our respondents were 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.

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