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Influence of Clinical Research Investigator Fraud on Clinical Trial Participation

Purnachandra Garimella, BPharm, MS[1,2], and Irwin G. Martin, PhD[1]

Abstract

The number of clinical research investigators that the US Food and Drug Administration has disqualified or totally restricted has been increasing since 1964. In addition, several public polls and surveys indicate a major dilemma in clinical trial participation and public perceptions of clinical research. This study investigates how clinical investigator fraud or misconduct influences public perceptions of participation in clinical trials. An electronic survey was developed for the faculty of Eastern Michigan University. The survey results (11.2% response rate) indicated that 81% of respondents were willing to consider participation in a clinical trial or had participated. However, when the respondents were told of a case of investigator fraud, approximately 25% of willing respondents were now discouraged from participation. The influence of the knowledge of investigator fraud did not seem to be greatly correlated with the geographic location of the event relative to the location of the respondents. While it seems that news of investigator fraud would therefore significantly affect enrollment efforts in ongoing clinical studies, these results reflect only a select group of highly educated people, and more definitive studies are recommended to understand the impact of investigator fraud and the duration of this impact on patient recruitment into clinical studies.

Keywords

fraud, clinical trials, recruitment, investigators

Introduction

This study examines the influence of investigator fraud on participation in clinical trials. This research may provide a better understanding of the negative impact of reporting on this misconduct without proper context.

The US FDA's Office of Regulatory Affairs (ORA) oversees inspections and enforcement actions. The ORA has a list of various categories of clinical investigators who have been completely "disqualified" or "totally restricted" from clinical investigations, or received necessary "enforcement actions" by FDA due to noncompliance with regulatory requirements. Investigators have been disqualified or restricted since 1964, although the first decade of this century has shown a significant increase in the number of impacted investigators. Total, 126 clinical investigators (from 1964 to 2010) have been disqualified by the FDA. In the past decade (from 2001 to 2010) the number increased to 42 investigators from an average of 24 the previous 3 decades.[1]

Although various guidance documents are available to aid clinical investigators, research misconduct remains a persistent problem. The rise in the number of investigators disqualified or totally restricted likely influences the general public's perceptions of clinical trials. A nationwide survey conducted by the Center for Information and Study on Clinical Research Participation (CISCRP) found that only a small percentage of participants considered clinical trials to be safe.[2] One challenge of clinical research is to persuade people that they will not suffer as a result of participating. Lack of trust in clinical investigators hinders this belief.[3] This study focuses on the effect on public perception of clinical research by investigator fraud and its influences on participation in clinical trials. We tested whether knowledge of fraud committed by a clinical research investigator might affect a person's likelihood to participate in a clinical study and whether geographic proximity to fraud cases may contribute to a person's reluctance to participate.

[1] School of Health Sciences, Eastern Michigan University, Ypsilanti, MI, USA
[2] IRBMED, University of Michigan, Ann Arbor, MI, USA

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Corresponding Author:
Irwin G. Martin, PhD, School of Health Sciences, Eastern Michigan University, Marshall Building, Ypsilanti, MI 48197, USA
Email: imartin2@emich.edu

Table 1. Survey respondents by age.

Age Group, y	No. of Respondents	%
21 to 30	8	5
31 to 40	22	14
41 to 50	38	25
51 and older	84	55
Total	152	100

Methods

An electronic survey was developed to obtain the views of faculty members of Eastern Michigan University (EMU). There are approximately 1,396 faculty members at EMU. These include 692 regular faculty, 97 lecturers, and 607 adjunct faculty members. All of these faculty members were sent an electronic survey with opinion questions having a 5-point Likert-type rating scale.[4] The eligibility for this survey was any member of the EMU faculty over age 21. Approval for the study was obtained from the EMU College of Health and Human Services Human Subject Review Committee. In the survey, the participants were asked 5 study-related questions, followed by 5 response options, concerning a case scenario of a disease or condition. The case scenario read, "You have a disease or condition. You are being treated adequately, but improvement is possible. You are informed of a clinical study of a new, but not yet approved drug." The participants were also asked demographic questions. The 5 response options represented, for each question, the extent to which clinical investigator fraud was likely to influence the respondent. The survey was closed 2 weeks after it was sent out. The survey database did not collect any information (such as IP addresses) that might identify participants.

The average weighted mean and standard deviation values were calculated for Likert-type scale questions.[4] Based on the responses to first survey question, the other 4 study-related questions were cross-tabulated.

Results

A total of 156 faculty members out of the 1396 surveyed completed the survey for a response rate of 11.2%. The percentages of responses from each college of the university were similar to the total percentages of faculty in each college. Only 3 participants refused to provide their demographic information. Of the respondents, 60% were female. The age of the respondents is presented in Table 1. These responses are, therefore, likely a representative sample of the total faculty population.

From question 1, participants' prior clinical trial opportunities, experience, and likelihood to participate in future clinical trials were obtained. As shown in Table 2, 20% of respondents had previous clinical trial experience, and 61% of the respondents would be willing to participate in the future, given the opportunity. On the other hand, 10% of respondents had had opportunities to participate but had chosen not to, and the remaining 10% of respondents would not consider participating.

Table 2. Clinical trial participation: past and future.

Q1: Previous Clinical Trial Participation	No. of Respondents	%
Those who had an opportunity and participated in clinical trials	31	20
Those who had an opportunity but DID NOT participate	15	10
Those who NEVER had an opportunity but will consider participating	95	61
Those who NEVER had an opportunity and WILL NOT consider participating	15	10
Total	156	100

Question 2 captures participant perceptions on the influence of investigator fraud on a clinical study conducted somewhere in the US. As shown in Table 3, 45% respondents report that investigator fraud somewhere in the US would not likely influence them. Conversely, the second-largest portion of respondents (21%) said fraud would very likely influence them.

The third question in this series asked about the extent to which respondents would be influenced by investigator fraud committed in the state of Michigan. Table 3 displays the percentages for all responses. In this case, 35% of respondents reported that Michigan investigator fraud would not likely influence their decision to participate in local clinical trials, whereas 23% of respondents reported that Michigan investigator fraud would very likely influence them. This type of fraud was somewhat likely to influence 17% of respondents, and 15% of respondents answered less likely.

The influence of local hospital investigator fraud on the decision to participate in a clinical trial conducted by another investigator was obtained from question 4. As summarized in Table 3, misconduct or fraud by an investigator at a local hospital would not likely influence 21% of respondents in deciding whether to participate in a clinical study by another investigator. Nevertheless, it would very likely influence 21% of respondents and moderately likely influence 22%. In addition, this misconduct would less likely influence 21% and somewhat likely influence the remaining 21%. Responses to this question were dispersed almost uniformly among all 5 options.

The influence of fraud committed by a patient's physician on respondents' likelihood to participate a clinical trial was determined from the last question. Table 3 shows that fraud committed by a patient's physician would very likely influence 79% of respondents. In addition, this type of misconduct would moderately likely influence 6%, somewhat likely influence 5%,

Table 3. Clinical trial participation versus extent of fraud's influence.

Fraud/Misconduct Response	Q1: Clinical Trial Participation				Total	
	With Experience	Would Participate	Didn't Participate	Wouldn't Participate	n	%
Somewhere in the US						
Not likely	18	37	8	6	69	45
Less likely	7	10	1	0	18	12
Somewhat likely	3	18	1	1	23	15
Moderately likely	2	6	2	2	12	15
Very likely	1	23	3	6	33	21
Total	31	94	15	15	155	
Michigan						
Not likely	15	29	7	3	54	35
Less likely	4	15	2	2	23	15
Somewhat likely	6	16	2	2	26	17
Moderately likely	4	9	0	3	16	10
Very likely	1	25	4	5	35	23
Total	30	94	15	15	154	
Local hospital						
Not likely	10	17	2	3	32	21
Less likely	6	18	3	1	28	18
Somewhat likely	7	14	5	1	27	18
Moderately likely	4	24	1	5	34	22
Very likely	3	21	4	5	33	21
Total	30	94	15	15	154	
Patient's physician						
Not likely	2	5	3	3	13	8
Less likely	1	1	0	0	2	1
Somewhat likely	2	5	0	0	7	5
Moderately likely	1	6	0	3	10	6
Very likely	24	77	12	9	122	79
Total	30	94	15	15	154	

and less likely influence 1%. This fraud would not likely influence 8% of respondents.

The survey respondents can be grouped according to the 4 major special classes of participation. It is illustrative to cross-tabulate the results of these 4 classes of respondents, since their responses to other misconduct or fraud questions differ significantly on certain fraud questions as shown in Table 3.

Cross-tabulated information among all 5 research questions presents an idea of data distribution among participants. The above table differentiates responses of all participants depending on their likelihood to participate in clinical trials. From the table, 3 major categories of respondents were chosen for discussion. Category 1 includes those participants who previously participated in clinical trials. Given their experience in clinical trials, their responses to fraud- or misconduct-related questions are significant. Category 2 includes those participants who would consider participating in future clinical trials if given the opportunity. Category 3 consists of those participants that have neither participated in the past nor wish to participate in the future. This latter category will not be discussed further for data analysis.

Of those responding, 20% were category 1 respondents—individuals who had participated in clinical trials before. The investigator misconduct or fraud somewhere in the US would not likely influence 58% of category 1 respondents. It would very likely influence 3% of category 1 respondents, which in this case means only one respondent. Investigator misconduct or fraud in Michigan would not likely influence 50% of category 1 respondents and would very likely influence 3% (again, only 1 respondent). Fraud in a local hospital would not likely influence 34% and would very likely influence 10% of category 1 respondents. Fraud committed by a patient's physician would very likely influence 80% of category 1 respondents and would not likely influence 7%. In sum, it appears that research fraud is not likely to influence most category 1 respondents, unless it is committed by the patient physician; research fraud by a patient physician is very likely to influence most of the category 1 respondents.

The survey respondents who would consider participating in future clinical trials (category 2) account for 61% of total

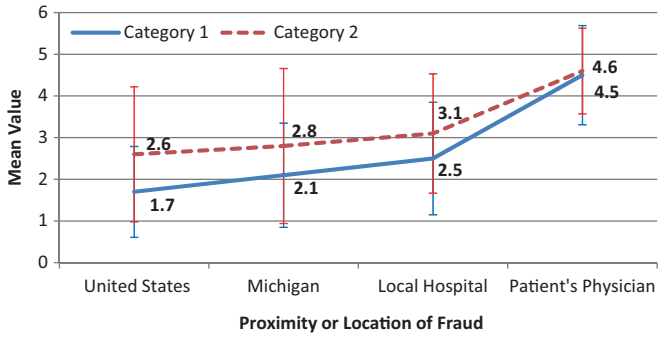

Figure 1. Mean values versus location of fraud for category 1 ("with experience") and category 2 ("would participate") participants.

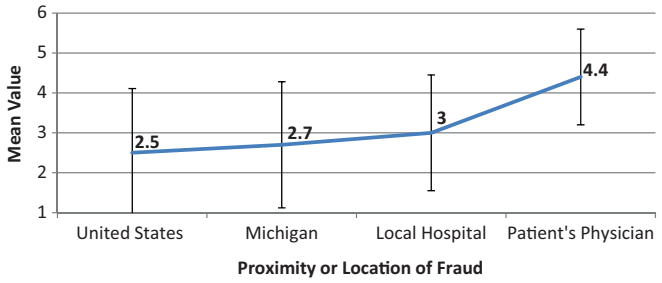

Figure 2. Mean extent of fraud influence by fraud location.

respondents. Investigator misconduct occurring somewhere in the US would not likely influence 40% of category 2 respondents, whereas 25% said fraud would very likely influence them. In cases of fraud in the state of Michigan and in a local hospital, category 2 respondents' answers differed. Fraud occurring in Michigan would not likely influences 30% of respondents, while 27% said it would very likely influence them and 17% said less likely. In contrast, fraud in a local hospital was not likely to influence 18%, less likely to influence 19%, somewhat likely to influence 15%, moderately likely to influence 26%, and very likely to influence 22% of respondents. Fraud by a patient's physician was very likely to influence 82% of category 2 respondents and moderately likely to influence 6.4%. Fraud committed by a patient physician would not likely influence 5.3% of respondents. In sum, the majority of category 2 respondents said fraud committed by a patient's physician would very likely influence them, while fraud somewhere in the US was not likely to influence them.

The likelihood of investigator fraud influence on a respondent's decision to participate in clinical trials was determined by calculating the mean of each section of response since the extent to which investigator fraud influenced respondents changed in each case, depending on the location of the investigator or fraud. Since these survey questions were designed and developed using a 1 (*not likely to influence*) to 5 (*very likely to influence*) Likert-type scale for responses, the mean for each question could be determined. Finally, the extent of investigator fraud influence in each of the 4 situations presented—somewhere in the US, in Michigan, in a local hospital, and by a patient's physician—was obtained. A graph drawn between category 1 and category 2, with these calculated mean values of fraud influence (with scale on y-axis: 1 = *not likely*, 2 = *less likely*, 3 = *somewhat likely*, 4 = *moderately likely*, and 5 = *very likely*) gives an exact and final distribution of investigator fraud influence (Figure 1).

Of the 33 respondents who said fraud occurring somewhere in the US would very likely influence them, 70% were in category 2. Of the 35 respondents who said fraud in Michigan would very likely influence them, 71.4% were respondents from category 2. Likewise, of the 34 respondents who reported that fraud in a local hospital would moderately or very likely influence, the majorities were in category 2. The category 1 responses to cases involving fraud committed in Michigan or somewhere in the US were constant, differing in fraud cases occurring in a local hospital or involving a patient's physician.

The mean values were calculated for all participants using the 1 (*not likely*) to 5 (*very likely*) scale. The graph drawn between mean values versus locations of investigator fraud did not give a significant increase in slope. However, from the graph (Figure 2) it appears that the average likelihood of fraud influence gradually increased the closer the proximity of the fraud, but increased greatly if the respondent's own physician was involved.

Discussion

The participants in this survey research were faculty members at EMU and therefore well educated, with doctoral or master's degrees. In addition, the population was diverse, including faculty from all colleges within the university. The majority of respondents (81%) were age 41 and older, and 55% of this segment were older than 50.

The majority of survey respondents stated that they would consider participating in other clinical trials, given the opportunity. Knowledge of fraud, irrespective of where it occurred, would discourage 25% of this group from participating in clinical trials. Therefore, it seems that knowledge of investigator fraud or misconduct, regardless of where it occurred, may very likely discourage the general public from participating in clinical trials. In addition, as investigator fraud occurs geographically closer to the respondents, they gradually grow less inclined to report that the fraud would not likely influence them. Of respondents who were interested in participating in clinical trials, 40% said that fraud occurring somewhere in the US would not likely influence them. The closer the geographic proximity of the fraud, the less often respondents reported that

knowledge of the fraud would not likely influence them: 31% if the fraud occurred in Michigan, 18% if the fraud in occurred in a local hospital, and only 5% if their own physician committed the fraud. Again, these values suggest that the location of a known instance of fraud affects respondents' willingness to participate in clinical trials. It is not geography, however, but the knowledge of fraud and of who committed it, that discouraged respondents from participating in clinical trials.

Wherever it may occur, research investigator fraud influences people's likelihood to participate in clinical trials. Those who have already participated in clinical trials were nearly consistent about their decision to participate when they heard about the investigator fraud. The perceptions of those who had never before participated but would consider participating in future changed with any fraud knowledge and also changed rapidly with their investigator fraud. On the other hand, all reports of willingness to participate followed immediately after learning of the existence of investigator fraud. How long this knowledge of a fraudulent event will have the public's or participant's attention is another important research question to consider. Hence, further studies are recommended to study the duration of this impact.

It appears that as the location of the investigator fraud approaches the location of the individual, its likelihood to influence that individual's decision to participate in clinical trials also increases, albeit modestly. However, the differences between the averages were small in cases of fraud occurring somewhere in the United States, in Michigan, and in a local hospital. The influence of fraud in these 3 cases is mild compared to the last case—fraud committed by a patient's physician. The influence of research investigator fraud or misconduct may depend on the location of the fraud, but this geographical impact is small compared to knowledge of fraud committed by a patient's physician.

Patient recruitment and retention is a constant challenge for clinical research organizations. To rise to this challenge, every organization must secure and maintain public trust and confidence in clinical research. The results from this pilot study show that knowledge of investigator fraud has a greater impact on the participant's perceptions than knowledge of where the fraud occurred. The present findings address only a select group of highly educated members of the community. Further studies involving larger populations are recommended to learn more about clinical research investigator fraud and its influence on the public perception of clinical trials. Additional data will be necessary to extrapolate these findings to other populations and to further understand the duration of fraud impact on recruitment into clinical studies.

Declaration of Conflicting Interests

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