Original Article

Evaluation of factors that act as barriers in conducting academic trials – An investigator's perception

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Abstract

Background: Academic trials are essential in investigating health research questions relevant to the society. Only a few leading research institutions in India have been engaged in academic trials. Thus, there is a need to understand what factors dampen the spirit of the academician in conducting academic clinical trials.

Aims and Objectives: The aim of the study is to evaluate the investigator's perception of obstacles to carrying out academic trials and to identify factors that will motivate investigators in conducting academic trials

Materials and Methods: We conducted a prospective observational study in a tertiary care hospital for 6 months. Faculty members working in academic institutes were selected. A structured questionnaire was designed for the study and administered using google forms. Responses were taken on a Likert scale. Validity and reliability assessments were carried out. Mann-Whitney test was applied to assess differences between demographic groups. $P < 0.05$ was considered significant.

Results: Most of the participants rated applying for research grants (76%), obtaining funding for the study and making arrangements for compensation for trial-related events (75%) as extremely challenging. We found that the degree of challenge is significantly lower in the faculty members who conducted clinical trials in the past as against those who did not (P = 0.00069). We also found that the degree of challenge is significantly higher in the faculty members with <10 years of experience than those with >10 years of experience ($P = 0.00001$).

Conclusion: Thus, to conclude the challenges faced by investigators were at multiple levels, most common being applying for research grants and making arrangements for the funds for payment towards participation or study-related injury. Faculty members with exposure to conducting clinical trials and with experience of more than 10 years had perceived a reduced degree of challenges.

Keywords: Challenges, infrastructure requirements, payment for participation, time constraints, training requirements, treatment and compensation of study-related injury

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INTRODUCTION

Academic trials or investigator-initiated studies (IIS) are clinical studies conceived, planned, and managed by individual physician–researchers or an institution or a group of collaborative clinical researchers or/institutions.[1,2] These trials are a valuable component of

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the health-care system; they benefit patients and help determine the safety and efficacy of drugs and devices and play an important role in the checks and balances as compared to regular commercially oriented clinical trials. IIS includes a wide range of studies – clinical trials of new drugs and real-world prospective or retrospective studies. IIS can help physicians in repurposing of drugs and in investigating health research questions relevant to their practice.[1] Data from real-world settings, generated by investigator-initiated trials, are more applicable to the population studied and can help in developing hospital/state/country-specific health guidelines and policies as compared to sponsored trials.[1,3]

Academic studies are the foundation of a country's clinical research strength. Data from ClinicalTrials.gov show that 239,401 registered clinical trials between January 1, 2006, and December 31, 2017.[4] Nonindustry academic sources that include the US National Institutes of Health and US federal agencies, individuals, universities, or organizations funded 65% of these studies. However, in India, the majority (61%) of the trials were industry funded.[4] It appears that Indian institutions are comparatively less enthusiastic about conducting academic clinical studies. This could be due to several challenges – financial, trained workforce, expertise in research methodology, and time constraints, among others.[5] Furthermore, lack of incentives and delay in ethical clearance, time, and infrastructure requirements could add to the challenges. The recently released the New Drugs and Clinical Trials Rules 2019 are likely to add to the burden of investigators interested in conducting academic clinical trials.[6] The challenges imposed by these could be bearing treatment and compensation of trial-related injuries.

Academic trials are essential to test the safety and efficacy of new treatments in certain populations. The paucity of drug trials has led to the widespread use of unlicensed or off-label medications, exposing them to the risks of drug toxicity and ineffective treatment.[7] In India, only a few leading research institutions have been engaged in academic trials or biomedical and health research.[4] Thus, there is a need to understand what factors dampen the spirit of the academician in conducting academic clinical trials. The study findings may help in providing recommendations for planning better conditions and resources that will facilitate academic clinical trials. With this background, we decided to evaluate the investigator's perception of obstacles to carrying out academic trials and to identify factors that will motivate investigators in conducting academic trials.

METHODOLOGY

Research design

A prospective observational study was carried out in a tertiary care hospital by the Department of Pharmacology, AIIMS, Nagpur, India.

Duration of study

The study was conducted over 6 months.

Ethics

The study was carried out after approval from the institutional ethics committee and carried out in accordance with Good Clinical Practice guidelines and the ethical principles as mentioned in the Declaration of Helsinki and ICMR guidelines. Electronic informed consent was taken from each participant. The study was not registered with CTRI as it was a survey-based observational study.

Sample size

There are no prior studies with similar objectives, and hence, we could not formally calculate the formal sample size. We decided to take a representational sample of 100 respondents.

Study procedure

Subject eligibility

The doctors working in tertiary care centers as faculty members of either gender and those consenting to participate were chosen. A structured questionnaire-based survey was carried out, and the questionnaire was circulated as a Google Form to ease the administration and reach out to more respondents.

Designing questionnaire

Various issues, challenges, constructs, and factors related to the investigator's perception about carrying out an academic trial were enlisted by the study team with the help of published literature. After deliberation from the study team, the self-administered, structured, and closed-ended questionnaire was designed. The responses were recorded using a Likert scale. The information related to the demography of respondents was also collected. Questions related to training and site requirements, workload balance, time constraints, infrastructure requirements, funds for carrying out trials, study procedures, and benefits related to carrying out studies were collected. The efforts taken for reducing bias were the removal of leading questions and removal of questions that might have similar responses. Issues such as simplification, error-free in construction, and grammatical errors also have been taken care at the review stage.

Measuring validity

The questionnaire was given to 10 experts to assess face validity. In order to examine the face validity, the dichotomous scale with the categorical option of "favorable" and "unfavorable" was used. The favorable item means that the item has clarity, comprehensibility, and good readability. The collected data were analyzed by Cohen's Kappa Index (CKI) to determine the face validity of the instrument. A minimally acceptable kappa of 0.60 for inter-rater agreement was considered acceptable. The face validity assessed by CKI was found to be 0.7.

Content validation was done by experts. The content validation experts were briefed to check the questionnaire items for their adequateness in measuring the constructs and to know whether the chosen items were sufficient to achieve the objective. The experts were asked to comment on the identification of any missed important items in the questionnaire and comment on the inclusion or removal of any questions which are not necessary for achieving the objective. The content validation ratio (CVR) was calculated using Lawshe's method.[8] CVR is the content validity ratio, n (e) is the number of expert panel members indicating "essential," and N is the total number of expert panel members. The content validity as measured by CVR was 0.9.

Measuring reliability

The questionnaire was administered to the sample respondents, and the respondents were instructed to score the items on the Likert scale. The questionnaire 1–25 was scored from 5 to 1 in the Likert scale, wherein 5 is very challenging and 1 is not challenging. Items 26–30 were scored in a reverse manner, where 1 strongly agree and 5 strongly disagree. Test–retest reliability was also carried out, where the questionnaire was administered to 10 respondents twice in a gap of 2 weeks. The reliability was evaluated using a correlation coefficient called Pearson's product-moment correlation coefficient (Pearson's r).[8] The test–retest reliability was assessed using Pearson's correlation coefficient, which was found to be 0.6.

Table 1: Demographic data of participants

Parameter	Frequency (%)
Gender	
Male	68 (68)
Female	32 (32)
Age (years)	
30–40	70 (70)
40–50	24 (24)
>50	6 (6)
Type of institute	
Government	94 (94)
Private	6 (6)
Number of participants who conducted clinical trial in the past	
Yes	17 (17)
No	83 (83)
Years of professional experience	
<10	61 (61)
10–20	27 (27)
>20	12 (12)

Statistical analysis

The data were summarized in percentages and frequencies. The responses were recorded using the Likert scale, and it was assessed for differences between demographic investigator groups, using Mann–Whitney *U*-test. $P < 0.05$ was considered statistically significant. The responses to questions 1–25 were scored from 5 to 1 on the Likert scale, wherein 5 is very challenging and 1 is not challenging. The analysis was performed using SPSS version 16 (IBM Corp., Armonk, NY).

RESULTS

A total of 178 faculty members across the state were approached, and 100 participants responded to the study questionnaire. Seventy-two percent of respondents were males and 28% were females [Table 1]. The majority of respondents (49%) were aged between 36 and 40 years. Most respondents worked in the government sector. About 17% of participants reported having conducted academic clinical trials and 83% had no experience in the conduct of academic clinical trials. Study participants with <10 years of experience were 61% and >20 years were 39%.

The details of the participants' responses are listed in Table 2. Most of the participants rated applying for research grants (76%), making arrangements for paying for participation in trial (67%), making arrangements for compensation for trial-related events (75%) extremely challenging, and ensuring no participant dropouts (69%) was rated highly challenging. Sparing time for research related work (54%), training site staff and investigators for conducting academic clinical trials (66%), designing protocol (63%), obtaining approval from the particular ethics committee (58%), and infrastructure related to storing specimens or drugs during the entire study (76%) was rated as moderately challenging by most participants. Study participants found the following aspects slightly challenging; writing a research paper (70%), integrating study-related procedures with clinical work; identifying, reporting, and managing adverse drug reactions (68%) and data collection procedures; and using appropriate analysis (57%). Most participants strongly agree that academic clinical trials aid in growth benefits, provide learning

Table 2: Degree of challenge perceived by the study participants (*n*=100)

Questions	Extremely challenging, *n* (%)	Moderately challenging, *n* (%)	Slightly challenging, *n* (%)
Training of investigators in protocol, GCP, and research methodology	22 (22)	53 (53)	25 (25)
Training of site staff in protocol and GCP	24 (24)	66 (66)	10 (10)
Sparing time between teaching undergraduate and postgraduate students	28 (28)	42 (42)	30 (30)
Sparing time from patient care	25 (25)	54 (54)	21 (21)
Sparing time from administrative responsibilities	28 (28)	46 (46)	26 (26)
Long and unpredictable working hours	30 (30)	53 (53)	17 (17)
Amount of time for appropriate literature search and finding key areas for research	49 (49)	30 (30)	21 (21)
Amount of time for designing protocol and other study-related documents	20 (20)	63 (63)	17 (17)
Amount of time taken for obtaining ethics committee approval	27 (27)	58 (58)	15 (15)
To know which research grants to apply	76 (46)	21 (21)	3 (3)
The timelines to follow when allotted a research grant	48 (48)	24 (24)	28 (28)
Making arrangements of funds for payment for participation to trial participants	67 (67)	29 (29)	4 (4)
Making arrangements of funds for payment toward treatment and compensation of trial participation	75 (75)	20 (30)	5 (5)
Assessing inclusion–exclusion criteria	20 (20)	15 (15)	65 (65)
Recruiting participants	16 (16)	25 (25)	59 (59)
Integrating study-related procedures with usual clinical care procedures	24 (24)	24 (24)	52 (52)
Ensuring study-related visits and protocol-related requirements are met	26 (26)	32 (32)	42 (42)
Ensuring no participant dropout	69 (69)	18 (18)	13 (13)
Understanding data emerged and appropriate analysis	16 (16)	27 (27)	57 (57)
Identifying and reporting the adverse events	7 (7)	25 (25)	68 (68)
Questions	**Strongly agree**	**Neutral**	**Disagree**
The conduct of academic trials provides learning opportunities	66 (66)	22 (22)	12 (12)
The presentation of academic trial findings has higher chance of winning awards at conferences	64 (64)	22 (22)	14 (14)
The paper on academic trial findings has a higher chance of getting published in high-impact factor journals	72 (72)	20 (20)	8 (8)
The conduct of the academic trial aids in academic growth and promotions	61 (61)	28 (28)	11 (11)
The conduct of the academic trial provides respect among seniors and peers.	80 (80)	19 (19)	2 (2)
Writing a research paper	12 (12)	18 (18)	70 (70)

GCP=Good clinical practice

Table 3: Comparison between the perceived degree of challenge among two demographic groups

	Degree of challenge
Conducted CT in the past (mean)	2.69
Not conducted CT in the past (mean)	3.22
Z score	3.6
P	0.00069
<10 years of experience (mean)	3.64
>10 years of experience (mean)	2.81
Z score	5.7
P	0.00001

CT=Computed tomography

opportunities, and bring respect and promotions in their workplace.

We compared the degree of challenge between the two demographic groups [Table 3]. We found that the degree of challenge is statistically significantly lower in the faculty members who conducted clinical trials in the past as against those who did not conduct clinical trials in the past ($P = 0.00069$). We also found that the degree of challenge is significantly higher in the faculty members with <10 years of experience compared to those who had more than 10 years of experience ($P = 0.00001$).

DISCUSSION

The study found that the most challenging of the tasks while conducting academic trials are to find the research grants for the study, make arrangements for the funds for payment for participation or the treatment or compensation of study-related injury, or ensure the retention of the participant in the study. The moderate challenge identified by the faculty members was training the study team, sparing time from patient care and teaching, the time required for designing study-related documents, and obtaining ethics committee permission. The tasks that were perceived to have the least challenges

were the aspects related to integral parts of conducting the study (assessing selection criteria, recruiting participants, and ensuring study-related visits, and protocol requirements were met). Other tasks that were perceived to have the least challenges were understanding data emerged and data analysis, reporting adverse events (AEs), and writing the research paper. Most faculty members agreed that conducting clinical trials provide learning opportunities, have higher chances of winning awards or publications in high-impact journals, aid in growth and promotions, and bring respect among peers and seniors. The degree of challenge is significantly lower in the faculty members who conducted clinical trials in the past compared to those who did not conduct clinical trials in the past. Furthermore, the degree of challenge is significantly higher in the faculty members with <10 years of experience compared to those who had more than 10 years of experience.

The most important challenge identified by the faculty members was to find the research grants for the study. The intramural grants fund the research carried out in academic institutes. The organizations such as ICMR, the of Biotechnology, Department of Science and Technology, and AYUSH provide extramural funds.[9] These agencies fund clinical research on their thrust areas of national importance. Applying to the funding agency means identifying their area of interest, the nature of support, following the guidelines given by them, and making a suitable and successful proposal for funding. This process may seem cumbersome to the investigator who is already short of time. A study conducted among dental professionals has also identified lack of funds as one of the most important hurdles in carrying out research in the field of dentistry.[8]

Arrangements for paying participants for participation or treatment and compensation for trial-related injury are an extremely difficult task. The guidelines recommend estimating the quantum of compensation which is similar to the pharmaceutical-sponsored clinical trials. The academic trials or IIS are conducted on a very limited budget.[10] The solutions that are offered are to make the budgetary provisions at the institutional level for the medical management of AEs and serious AEs (SAEs) such that the compensation costs are covered. The funding bodies could be the institutes intramural funds or the investigator may apply to governmental or nongovernmental agencies or self-funding.[1] Many of these funding agencies do not provide for expenses toward treatment and compensation for trial-related injury as the exact expenses cannot be predicted before initiation of the study and accounted for in the budget. Thus, taking the onus for paying for treatment and compensation of study-related injury may hamper the conduct of academic trials, which answer very pertinent questions that have a direct impact on society.[11]

One solution to this issue is to make provision of insurance to trial participants.[12] However, then the onus of payment will rest with insurance companies who must settle the case as per their procedures and in the requisite timelines. The investigators and study team will need to follow-up with the insurance companies for the due payments. Furthermore, one cannot deny that the insurance premiums in research in critically ill patients may be very high and may not be covered by intramural or extramural grants and is out of the question for self-procurement by academicians.[12]

The moderate challenges identified were training the staff in research methodology and the study protocol. In a pharmaceutical-sponsored study, these responsibilities are taken up by the sponsor; however, these become integral responsibilities of the investigator in the academic trial and can be overwhelming. A study conducted by Paramasivan et al identified research gaps from published studies on research ethics in India, this study found that education and training of personnel on clinical trials and research ethics as one of the important research gaps.[13] Furthermore, a study by Parikh *et al*., which is an online survey was conducted among various stakeholders from the clinical drug trial industry in India, confirmed that urgent steps need to be taken in terms of proper training of all stakeholders.[14] A study conducted by Franzen *et al*., that evaluated barriers and enablers identified funding and fewer learning opportunity and limited human capacity as important barriers to conducting academic trials.[15] Interestingly, the enablers identified were training, knowledge sharing, experience exchange, and practical collaborative support.[15]

Other perceived moderate challenges were sparing time from routine activities, designing study-related documents, and obtaining ethics committee permission. The lack of time is one of the important aspects that can be dealt with by having adequate workforce and a reduction of workload. This will result in sparing some time for other activities. In agreement with our study, Sivanandan *et al*., provide the experience of investigators and the challenges faced during the conduct of the trial in neonates.[7] Time constraints associated with the documentation of written informed consent, reporting, and follow-up of SAEs have been identified as one of the challenges. Furthermore, delay in ethical clearance can be of concern, especially in a

multicenter trial or if conducted in vulnerable subjects. This may be because the onus of the academic trials lies with the ethics committee and regulatory bodies do not have much role to play. Thus, ethics committees tend to be extra cautious in giving approvals and may raise questions related to how the treatment and compensation of study-related injury will be taken care of.

The aspects of conducting the study that are assessing selection criteria, recruiting participants, and ensuring protocol-related visits were identified as less challenging. This could be due to our country's large patient pool of various diseases.[16] Furthermore, the availability of mobile phones has reduced the burden of reaching out to other people and mobile reminders have improved compliance to visits.[17] The data analysis has been perceived as less challenging because the analysis component is usually dealt with by a statistician who is either present in the institute or is approached by investigators. Similarly, writing the manuscript can be cumbersome; however, it is dependent on the investigator and it can be accomplished if adequate time is devoted.

The advantages of conducting academic clinical trials are well appreciated by the faculty members. In an academic trial, the responsibility of developing a protocol and other study-related documents, monitoring, data analysis, interpretation, etc., lies with the investigators.[18] These are not the responsibilities of the investigator while carrying out the sponsored clinical trial. Thus, investigators perceive the entire process to be very highly rewarding. Furthermore, the interventional studies carried out as a part of these have a high chance of getting published in a journal with a high-impact factor compared to case reports and observational studies.

The strength of our study is that there are no Indian studies that have evaluated the perception of challenges faced by investigators in conducting academic clinical trials. The limitation of our study is that we have a limited sample and most of our sample is faculty members working in the government sector. However, the challenges perceived may not change drastically for faculty members working for private institutes.

CONCLUSION

Thus, to conclude, the challenges faced by investigators were at multiple aspects. Most commonly include challenges in applying for research grants and making arrangements for the funds for payment for participation or treatment and compensation of study-related injury. Most faculty members appreciate that clinical trials provide learning opportunities and are rewarding in terms of publication in high-impact journals or helping in growth and promotion. Faculty members with exposure to conducting clinical trials and with experience of more than 10 years had perceived a reduced degree of challenges. Thus, it is necessary to make a research-conducive environment by supporting the academicians financially and assisting them in capacity building.

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Conflicts of interest

There are no conflicts of interest.

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