Results of an Online Survey of Stakeholders Regarding Barriers and Solutions to Clinical Trial Recruitment

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CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

Abstract
Objective: The objective of this abstract is to describe the results of a multi-stakeholder survey designed to obtain a deeper understanding of stakeholders' perceived barriers and suggested solutions to clinical trial recruitment (CTR).

Method: A web survey of 300 stakeholders (90 patient advocates, 90 clinical research sites, 90 US and global investigators and 30 sponsors) was opened for 30 days on 7/15/14. Snowballing (forwarding the survey to persons not included in the original sample) was allowed. 90 completed surveys were analyzed.

Results: CTTI surveyed stakeholders about barriers to and methods for improving CTR, organizational experience with various methods, personal outlook on the future of CTs, and which partnerships would be most effective in increasing CTR. The most significant barrier to CTR was the ability to find subjects who meet study criteria. The next most significant barriers were insufficient staff time for recruitment activities, followed by the length and complexity of consent forms, and protocol requirements other than eligibility criteria. Other less significant barriers included patient mistrust of research, scheduling difficulties, transportation, out-of-pocket expenses, negative attitudes toward clinical research among referring physicians, patient concerns about randomization or study design, patient concerns about safety, and social stigma associated with enrollment for a disease or condition. Suggestions to overcome CTR barriers included broadening eligibility criteria, planning, use of effective methods and technology, education, improving staff support for CTR, reducing the length and complexity of consent forms, simplifying study design and considering alternatives to on-site visits. CTR through the use of medical records or hospital-based registries/databases was felt to be most effective and most often successfully employed by respondents. Regarding outlook on the future of CTs in the next 5-10 years, slightly more respondents were optimistic than pessimistic for both the 5 and 10-year marks. When asked what combination of sectors would be most effective in partnership to increase CTR, patient advocates and sponsors were named most often. The two most often mentioned partnerships were 1) patient advocates and researchers and 2) broader coalitions between patient advocates, government regulators, researchers, sponsors and professional societies. Because of the use of snowballing to increase the number of respondents, the actual response rate cannot be known.

Conclusion: Survey respondents were more likely to be executives or senior staff with >10 years of CT experience, leading to concerns that respondents may have been too far removed from day-to-day operations to have an accurate understanding of recruitment barriers. Survey results indicated a significant reliance on technology for improving CTR, such as the use of electronic health records (EHRs), hospital-based registries and databases and electronic alerts to CT staff. This raises the question of whether investigators and study designers are relying on the increased availability and use of technology (EHRs, registries, e-alerts) to make it acceptable to increase the complexity of research protocols and whether the use of such technology may just be automating a broken process that requires more comprehensive changes to improve CTR. Additional questions remaining include whether and how study sponsors and staff plan and execute recruitment plans, including the engagement of appropriate partners (patients, advocates, providers and payers), identification of appropriate sites with access to the available population, the development of realistic timelines through the use of appropriately designed feasibility studies and how to use marketing strategies to improve CTR and education about the importance and availability of clinical research in the general public.

Introduction

A staggering number of clinical trials fail to meet recruitment goals, which leads to delays, early trial termination, or inability to draw conclusions at trial completion due to loss of statistical power. A recent analysis found that 19% of registered trials that closed or terminated in 2011 either failed to meet accrual goals or were terminated early due to insufficient accrual.[1] Insufficient recruitment can have ethical implications for participants, result in missed opportunities for patients who can benefit from clinical trials, and waste time, funds, and other resources. The Clinical Trials Transformation Initiative (CTTI) launched the Recruitment Project to identify and propose possible solutions to barriers in clinical trial recruitment.

After reviewing available evidence in the literature, the project team designed a survey to obtain a deeper understanding of stakeholders' perceived barriers to recruitment across the clinical research enterprise. The objective of the survey was to gather information for the future development of recommendations and approaches that will improve patient recruitment and enable trials to meet their recruitment goals.

Methods

The CTTI Recruitment Project Team developed a 15-minute online survey to gather information on barriers to clinical trial recruitment, methods for overcoming these barriers, organizational experience with various recruitment methods, partnerships that would be most effective in increasing recruitment, and stakeholder outlook on the future of clinical trial recruitment.

The survey was determined exempt from human subjects review. On July 15, 2014, an email invitation was sent to 300 sample members identified by the project team, comprising 90 patient advocates, 90 sites, 45 global investigators, 45 investigators, and 30 sponsors. Data were collected for one month, during which time a reminder message was sent to encourage participation.

Sample members were permitted to forward the survey link to colleagues, and the survey was also publicized via CTTI-affiliated Twitter accounts. Due to the snowballing sampling method, the eventual sample size for calculation of a response rate cannot be known. The survey was anonymous, and no incentive was provided for participation. A thematic analysis was conducted of the responses to the open-ended survey questions using standard qualitative techniques.

Results

Data from 90 completed surveys were included in the analysis. Completed surveys may have some missing data because item nonresponse was permitted. A breakdown of respondents by organization type is presented in Table 1. Overall, 70% of respondents reported having significant influence in determining recruitment strategies for the trials they manage. Many were executives or senior staff with more than 10 years of experience in clinical trials.

Barriers to Recruitment

A key goal of the survey was to collect opinions about the significance of various barriers to clinical trial recruitment. Respondents were asked to rate each named barrier as very significant, somewhat significant, minor, or not a barrier at all. The barrier rated by the most respondents as very or somewhat significant was that of finding or identifying patients who meet eligibility criteria (Table 2).

Respondents from sponsors and clinical research organizations (CROs) more commonly rated finding patients who meet eligibility criteria a significant barrier (92%-95%) than did respondents from research sites and patient advocacy groups (78% each).Transportation to trial visits and out-of-pocket expenses were more often rated as significant barriers by respondents from patient advocacy groups (56% and 67%, respectively) than sponsors, CROs, and research sites (21%-47%).

For each barrier that was rated as "very significant" or "somewhat significant," an open-ended follow-up question was asked: "From your perspective tell us briefly how this barrier can be overcome or what steps have been taken by your organization to overcome this barrier." Table 3 shows a summary of the most frequent recommendations for overcoming each of the named recruitment barriers. Another component of the survey assessed respondents' perceptions of specific methods to improve recruitment (Figure 1).

Table 1. Respondents by Organization Type (N=90)

Organization Type	n (%)
Academic research organization	24 (26.7)
Industry: pharmaceuticals	17 (18.9)
Patient advocacy, no sponsorship of trials	14 (15.6)
Clinical research organization	12 (13.3)
Patient advocacy, including sponsorship of trials	7 (7.8)
Federal government: research (NIH, VA)	6 (6.7)
Something else	4 (4.4)
Clinical research site	2 (2.2)
Industry: biotechnology	2 (2.2)
Federal government: regulatory (FDA)	1 (1.1)
Industry: medical devices	1 (1.1)

FDA, US Food and Drug Administration; NIH, National Institutes of Health; VA, US Department of Veterans Affairs.

Table 2. Barriers Rated Very or Somewhat Significant

Barrier	Percent[a]
Finding or identifying patients who meet eligibility criteria	81.1
Insufficient staff time for recruitment	67.4
Length and complexity of consent forms	65.6
Protocol requirements other than recruitment criteria	60.3
Patient mistrust of research	45.6
Difficulty scheduling study visits	40.5
Transportation to study visits	45.0
Out-of-pocket expenses	41.5
Negative attitudes among physicians about referrals to clinical trials	39.8
Patient concerns about randomization or study design	36.7
Patient concerns about safety	33.0
Social stigma associated with enrollment for a disease or condition	7.8

a N ranged from 88-90 for each barrier rated.

Figure 1. Respondents' Belief That the Named Methods Can Improve Recruitment

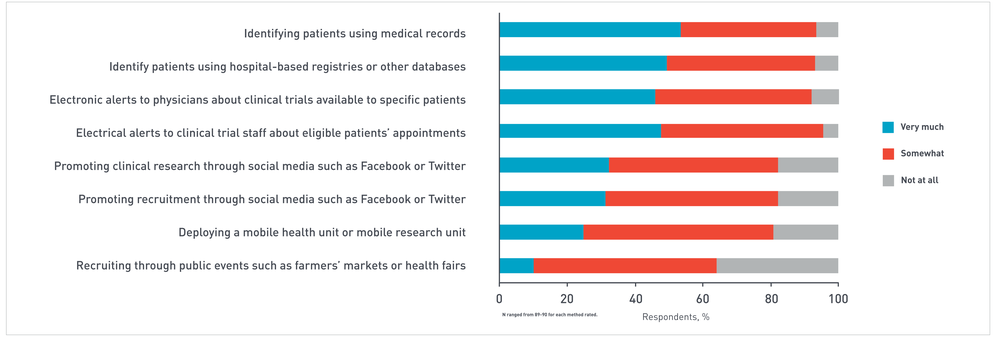


Table 3. Respondent Recommendations for Overcoming Recruitment Barriers

Barrier	Recommendations	Barrier	Recommendations
Finding/identifying eligible patients	• Broaden eligibility criteria • Engage in effective study planning, including site selection and development of recruitment strategies • Employ effective recruitment methods and technology (e.g., electronic health records, registries, referral programs) • Use education/advertising to increase public awareness of clinical research and help establish partnerships with providers	**Financial/logistical barriers: difficulty scheduling study visits, transportation to study visits, out-of-pocket expenses**	• Offer financial assistance (e.g., parking vouchers, travel reimbursement, compensation for missed work) to alleviate burden; include in study budget or find alternate funding sources • Use a simplified or alternate study design with in-home visits, visits during non-working hours, or reduced number of visits • Establish study sites at convenient locations and offer assistance with planning and scheduling visits, including travel • Allow flexibility in time window for study visits • Eliminate waiting time for seeing research staff, including principal investigator
Insufficient staff time for recruitment	• Improve site commitment to staffing: hiring, use of flexible staffing models, dedicated staff for projects • Increase financial support for research • Engage in appropriate advance planning (e.g., staffing budget, workload assessment, realistic recruitment timelines)	**Negative attitudes among physicians about referrals to clinical trials**	• Increase education about specific trials and general education on the importance of research to the health of society • Establish regular communication between physicians and researchers, involve physicians in the research process, and ensure that research does not impede clinical workflow • Encourage patients to ask their physicians about trials, and consider financial incentives for referrals
Length and complexity of consent forms	• Improve consent process: train staff obtaining consent and use interactive/multimedia tools to evaluate participant understanding • Simplify consent forms by eliminating redundancy, using plain language, and focusing on key issues related to the decision • Divide consent form into multiple parts, provide a synopsis of key points, or use a shortened form and provide a long version to take home • Tailor consent form to individual patients • Standardize IRB approaches across sites or use a central IRB • Lobby for broader changes in regulatory and sponsor requirements	**Patient concerns about randomization or study design and safety**	• Educate patients about randomization, placebo, standard of care, study oversight, and safety procedures • Consider alternate design methods (e.g., adaptive, crossover) to give best access to new treatments; reduce use of randomization or placebo • Ensure the consent process is properly carried out, including sufficient time for questions and discussion of concerns • Educate research teams on how to speak with patients about safety and potential risks
Protocol requirements other than recruitment criteria	• Simplify study design by eliminating visits and procedures not essential to study objectives • Evaluate protocols for feasibility: include patient input in study design and conduct pilot testing before implementation • Consider alternatives to main site visits (e.g., home visits, phone check-ins, remote monitoring devices) • Combine trial-related visits with personal medical visits	**Social stigma associated with disease or condition**	• Education • Maintain confidentiality
Patients' mistrust of research	• Education (e.g., webinars, media campaigns, "meet the investigator" forums) to increase awareness of safeguards in research and public benefits of research • Involve patient advocates and community members who can relate to specific groups in community outreach • Solicit patient input when designing research project (i.e., community participatory research)		

IRB, institutional review board.

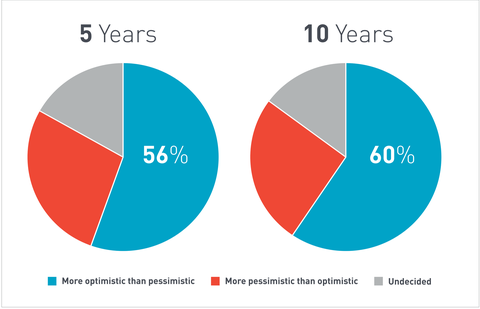
Effective Partnerships for Increasing Recruitment

When asked to identify what combinations of sectors would be most effective in partnership to increase clinical trial recruitment nationally, patient advocates (82%), sponsors (71%), and researchers (68%) were named most often. The two most frequently mentioned sector combinations were (1) patient advocates and researchers, and (2) broader coalitions between patient advocates, government regulators, researchers, sponsors, and professional societies.

Outlook on Increasing National Clinical Trial Recruitment

More than half of respondents reported a positive outlook for increasing national clinical trial recruitment rates over 5 and 10 years (Figure 2). When results were examined by organization type, patient advocates were the most optimistic group, with 70% and 74% reporting more optimism than pessimism for the next 5 and 10 years, respectively.

Figure 2. Outlook on Increasing National Clinical Trial Recruitment Rates in the Next 5 (N=90) and 10 Years (N=89)



Discussion

Results of the stakeholder survey indicate that there are significant protocol-related, patient-related, and clinician-related barriers to clinical trial recruitment, and there is no single solution for overcoming them. Respondents offered a variety of recommendations for improving recruitment that could be implemented at various stages of the research process, including during planning, recruitment, or throughout a trial, as well as some actions that could occur independent of any specific trial. These data have informed the work of the CTTI Recruitment Project, which will continue to engage stakeholders in understanding barriers to clinical trial recruitment and developing practical tools to address them.

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