Scientific Research Publishing

International Journal of Clinical Medicine, 2022, 13, 253-261
https://www.scirp.org/journal/ijcm
ISSN Online: 2158-2882
ISSN Print: 2158-284X

The Role of Recruitment and Retention in Clinical Trials

Alycia M. Ketter, Terry L. Oroszi

Department of Pharmacology & Toxicology, Boonshoft School of Medicine, Wright State University, Dayton, USA
Email: alycia.ketter@wright.edu

How to cite this paper: Ketter, A.M. and Oroszi, T.L. (2022) The Role of Recruitment and Retention in Clinical Trials. *International Journal of Clinical Medicine*, **13**, 253-261.
https://doi.org/10.4236/ijcm.2022.137021

Received: April 19, 2022
Accepted: July 15, 2022
Published: July 18, 2022

Abstract

It is evident that both recruitment and retention play critical roles in clinical trials. Recruitment and retention models are beginning to be analyzed worldwide in an effort to assess how to conduct studies more efficiently, all the while, allowing researchers to provide sound and ethical data to help advance medicine through clinical studies. Sponsors and sites have recognized that clinical trial enrollment must become more diverse and inclusive. In this review, we address the important topics of recruitment and retention in clinical trials. Specifically, the obstacles in regard to recruiting vulnerable populations. Methodologies to improve both the understanding of the study population and community engagement are outlined. In particular, newer strategies such as use of social media and more reliable strategies such as trust and relationship building are described in detail. A strong focus on recruitment is becoming widely recognized as being of such importance that consideration is given to this key component even during initial protocol development. Attention to recruitment and retention in the strategic planning process of clinical trials can mitigate enrollment issues that clinical researchers are experiencing.

Keywords

Recruitment, Retention, Clinical Trials, Enrollment, Study Population, Inclusivity, Diversity, Social Media

1. Background

Researchers are realizing that traditional recruitment and retention processes are no longer the most effective way to enroll clinical trial subjects, particularly in regard to diversity and inclusivity. Recruitment and retention are topics that need continued attention to help us better understand the populations needed

for each study. It is an area of focus that still requires much research to be done and a focus on utilizing the ever-changing technology that is available to us. In considering the future of clinical trial recruitment, researchers have identified that the internet and social media will play a vital role in the future of subject and site interactions.

1.1. Human Subject Research

It is necessary to understand how human subjects are defined and how far clinical trials have come over the years. The history of human research reveals that there have been a number of unfortunate scandals. Due to this history, there have been several safeguards put into place to protect and advocate for human subjects. Today, all credible agencies in the field of *clinical research* use the definition of a human subject, created by the U.S. Department of Health and Human Services:

(e)(1) Human subject means a living individual about whom an investigator (whether professional or student) conducting research: 1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or 2) Obtains, uses, studies, analyzes or generates identifiable private information or identifiable biospecimens (§46.102 e.1.) [1].

This classification helps researchers categorize a human subject to better protect them from mistreatment. It also helps essential agencies such as the Food and Drug Administration (FDA), National Institutes of Health (NIH), and Institutional Review Boards (IRB) to remain consistent in their definition of human subjects [1].

Institutional Review Board (IRB) for Recruitment

Institutional Review Boards (IRB) are responsible for reviewing patient-facing study information to protect study participants' human rights and welfare. They ensure that ethical standards are met and followed. IRBs were introduced and became a requirement in 1975 after unethical clinical trials negatively impacted many lives. Now, IRBs help to ensure human subjects are treated ethically and are appropriately informed of all study details [2].

1.2. Clinical Trial Recruitment and Retention

Recruitment and retention of human subjects in clinical research is a multifaceted topic. It is a topic that is potentially one of the most crucial aspects of the clinical trials process. Trial recruitment is as essential for the clinical trial process as the subjects themselves. Not only are human subjects a requirement, but there is usually a defined number of subjects required for each clinical trial. Subject retention is also a critical factor because, once they have completed a trial, they often choose to participate in subsequent trials that are available to them. From what I have encountered in clinical trial recruitment and retention, most strategies can apply to both recruitment and retention. However, it is evident that it is harder to build a relationship than it is to maintain one.

2. Methodology

2.1. Recruiting Vulnerable Populations for Clinical Trials

Recruiting youth can be a difficult feat. You not only have to receive the assent of the minor, but you are also required to obtain the consent of one or both parents, or the child's guardian. To reach multiple generations, the trial must have aspects that catch the eye of these two vastly different age groups which can be quite challenging. Enrollment success depends on perceived benefits from participating in the study, whether that is relief from their condition, health monitoring, or other benefits that may result from study participation. A majority of common struggles are time demands, unstable living conditions, comprehension, and communication issues such as language barriers. However, data shows that the most successful components of recruiting minors are establishing trust, creative advertising, and monetary incentives [3].

Numerous sites have turned to recruitment strategies that focus on offering monetary incentives due to the success seen with school-based sites. Another key incentive in recruiting adolescents is when studies offer free comprehensive health screenings followed up with a detailed explanation of the results from a health care provider. Technology-based incentives and online advertising primarily on social media platforms have also proven to be effective. Trust building is interesting when concerning pediatric and adolescent recruitment because the site staff not only has to gain the trust of the potential subject, but also the trust and confidence of the parents or guardians [3].

Active strategies tend to be the most effective when recruiting children. Active strategies include physician referrals and targeted mailings. Physician referrals usually result in an enrollment rate of just over 50%. Referring physicians reflect more successful enrollment numbers when they are familiar with the inclusion and exclusion criteria. In addition, these referrals typically require consistent communication with providers and their staff to ensure that the studies remain a priority to the patient. Targeted mailings, however, usually have a hefty cost attached and result in roughly a 30% enrollment rate [4].

Passive recruitment strategies include advertisements such as having an internet presence, word of mouth, and newspaper, bus, and television advertisements. Surprisingly, of all the active recruitment strategies, newspaper advertisements are the most valuable and unfortunately, the most expensive. The enrollment rate is at about 5%, so you can see that active strategies yield much better results in regard to enrollment numbers [4].

Social media is becoming more embedded into our everyday lives as time progresses, and sites are beginning to take advantage of this tool in recruiting for clinical trials. A study was conducted in 2017 to try to mitigate the additional burden that recruiting minors presents in trying to gain assent and consent [5]. They detailed the use of Facebook ads and traditional mailings in recruiting adolescent females for a drug prevention trial. The results suggested that Facebook did prove to be useful as an initial point of contact, and it is a cost-effective

recruitment tool. This tool can be helpful if used properly, however it does require vigilant monitoring of campaigns, and it has risks [5].

When it comes to recruiting elderly patients, there are often obstacles that arise. Older adult recruitment takes research staff more time to recruit than with the general population. Based on data collected in regard to the recruitment of older adults, the majority of these elderly patients were more inclined to participate when they had cultivated relationships with community-based organizations and recruiters that met the candidates face to face prior to signing the informed consent. They also had greater success when the study sites offered to provide services such as blood pressure checks to assess the eligibility of participants [6].

2.2. Diversity in Clinical Trial Recruitment

In the field of clinical research, it is a known fact that there is not a whole lot of diversity in study participants. It is also a fact that many are now making this issue a priority. Part of this lack of diversity stems from unethical trials of the past. The dark history of clinical trials unfortunately sticks with people to this day. Getting past this barrier requires a little historical context. If looking only at African Americans, historically, there is an extensive list of unethical human experimentations. The Tuskegee experiment is one of the most well-known human research events that a number of people associate with clinical research even today [7].

Research by Dennis and Neese (2000) suggests that minorities continue to be less insured than their white counterparts [7]. The inequality and lack of inclusivity can hinder minorities from participating in clinical trials and should be taken into consideration when recruiting for clinical trials. Another issue to consider is research bias. Research bias is another barrier that holds us back regarding diversity in clinical trial enrollment. Research is supposed to be based on sound scientific rationale; however, research protocols can be biased toward specific populations. The inclusion and exclusion criteria should be clearly stated and in great detail, leaving no room for confusion or doubt. Larson (1994) found that out of 754 protocols from her institution, about half of them had age exclusions and a majority of them did not have clear justifications [8]. The race of the participant was least likely to be an exclusion criterion; it was, however, along with age and socioeconomic status, linked to unexplained exclusionary criteria for studies [8].

Dennis and Neese (2000) outline six concepts that have developed as fundamental to research involving diverse groups:

1) historical cognizance; 2) sanctioning; 3) trust-building; 4) recognition of group heterogeneity; 5) mutuality; and 6) researcher self-reflection and introspection.

These concepts, if implemented along with planned strategies, can prove to be quite successful in working with diverse populations [7].

3. Recruitment Challenges

Recruitment does not often receive support or praise throughout the study process. When it comes to the study budget, recruitment is often an afterthought. This oversight results in sites being unable to meet their enrollment goals. Common causes for such shortcomings are that 1) sites do not create a recruitment strategy early in the process, 2) community members are not engaged, resulting in a lack of knowledge, and 3) lack of trust in the research team and clinical trials in general, which can sometimes be due to cultural differences.

Though there are various limitations that can hinder study enrollment, distrust is one of the most significant barriers for research sites all over the world. Study design, inconvenient locations, visit times, low compensation, education, lack of transportation, and a participant's general lack of interest in the study are also factors. All of these challenges make it difficult to recruit subjects. Still, thanks to research, there is data that shows us what effective strategies look like and how we can overcome these barriers to increase volunteer patient enrollment in studies.

4. Effective Recruitment Strategies

Combinations of recruitment techniques are used in clinical research every day. These techniques include clinic and hospital outpatient and inpatient referrals, patient database searches, community provider referrals, distributing flyers, newspaper advertisements, field-based recruitment and more. Field-based recruitment methods such as community outreach can include patient education events and campaigns. Recently, researchers have taken notice that community outreach is a crucial piece of the recruitment puzzle. Community outreach, field-based recruitment, and referrals are methods that are becoming strongholds in recruitment practices [9].

4.1. Knowing the Target Population for Clinical Trial Recruitment

In the past, recruitment was being given a one size fits all model; however, researchers have discovered that this theory is not sustainable in this day and age. Better knowing the populations that are being recruited will help to increase overall recruitment success. Recruitment specialists must now cater their recruitment strategy to the target population based on each protocol for more effective results [10]. Even so, the protocol procurement phase should involve thorough consideration of recruitment. It should also be completed with a clear idea as to who the population is in regard to the study that is being developed. One way to achieve this is to include the expertise of a recruitment specialist in the protocol development process.

4.2. Community Engagement

Community engagement is a crucial aspect of not only knowing your target population but also building trust with community members. Anastasi, Capili,

Kim, & Chung, (2005) noted that having a relationship with community servants in the field of study can help researchers gain the information they would not have otherwise [10]. A New York City research team had built a relationship with the Healthy Life Choices Project (HLCP). HLCP was able to inform the research team that a great deal of participants struggled with transportation costs, so the research team will begin to accommodate these costs in the future by adding travel reimbursements to their study budgets [10].

Being involved in the community can provide feedback such as transportation needs, appointment time flexibility, study materials not being easy to understand, and insights into what the community members value. When you engage the community's target populations, it can help you build trust and, in turn, improve enrollment [11].

4.3. Trust Building

Trust is something that is not only built but also maintained [12]. Based on a multitude of evidence, establishing trust between researchers and participants is crucial in human subject recruitment and enrollment. Building trust can be done by openness, providing a sense of security and comfort, and even expressing genuine gratitude [6]. It is necessary to increase trust and transparency throughout the research process because it is associated with participants' willingness to participate in studies [13]. Trust is more vulnerable during transitions. Usually, these transitions occur from care providers to research staff [12].

Swift Trust

Swift trust begins when a patient is referred to a site, during the recruitment process, and even during treatment phases of a study. It develops in temporary systems with patients, their loved ones, community providers, and with research staff interactions. It focuses on expectations and assumptions that people are dependable and capable. Recruitment is stressful as it is and there is added pressure due to time constraints that force the study team to make quick decisions with the information that is available to them. These time constraints sometimes also require the participants to make quick decisions and judgment calls with the lack of a relationship to support such decisions [12].

Within swift trust, there are five types of trust. *Ex-ante* refers to a referring physician that initiates trust between the participant and the research team. *Role-based* trust is trust that is solely based on an assumption of trustworthiness due to the researcher's position. *Rule-based* trust focuses on the hierarchy within the research team members in which they frequently interact. *Dispositional* trust refers to an individual's disposition, typically based on what they believe or how they carry themselves. *Category-based* trust focuses on one's identity or stereotypes [12].

Traditional Trust

Traditional trust usually comes following swift trust because it gradually develops over time. This form of trust can be considered knowledge based. It con-

siders a person's behavior and grows based on familiarity experience [12].

Within *traditional* trust, there are four stages of trust. *Calculus-based* trust is a simple form of trust as it is task-oriented. *Knowledge-based* trust is developed through deeper familiarity and interaction. *Affect-based* trust is formed based on reciprocated care and concern. *Identification-based* trust is built by understanding desires and intentions. It is usually socially driven and develops over time [12].

5. Discussion

Recruitment and retention for clinical trials is a multifaceted beast that has its difficulties along with its benefits. Underenrollment in clinical trials wastes resources and delays the discovery or development of new treatments [14]. After the review of data and statistics regarding recruitment and retention, it is clear that trust is a significant barrier. That being said, it is also one of the most popular strategies used to enroll minors, older adults, and underrepresented participants.

Recruitment and retention practices and their impact on clinical trials is complex. Many are using a limited number of tactics that considered to be traditional. Despite the wide variety of novel solutions available to sites, traditional approaches including use of physician referrals, radio and television advertising are most prevalent, whereas social media is just now beginning to be used on a global scale. Centralized recruitment is another nontraditional tactic that has proved to be an effective tool in recruiting clinical trial participants. More sites are beginning to incorporate solutions to recruitment issues that do not follow the traditional strategies but are effective and supported by increased enrollment numbers [15].

6. Conclusion

My hope is that all of the new research will put a spotlight on recruitment and retention in clinical trials, giving it the attention it deserves, in the world of research. Tracking metrics and specific organized recruitment methods should be commonplace, and models should be provided to the study staff at the site level. Despite the additional attention placed on recruitment and retention in clinical trials, there is still much to accomplish. The extra attention has opened countless doors in the field, though the industry would advance even further if those doors led to new recruitment and patient management platforms that could track studies, their recruitment metrics, and regulatory documents. Improvements like this would significantly impact the advancement of effectively recruiting and running clinical trials.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Department of Health and Human Services (2020) Definition of Human Subjects Research. https://grants.nih.gov/policy/humansubjects/research.htm

[2] Grady, C. (2015) Institutional Review Boards. *Chest*, **148**, 1148-1155. https://doi.org/10.1378/chest.15-0706

[3] Nguyen, T.T., Jayadeva, V., Cizza, G., Brown, R.J., Nandagopal, R., Rodriguez, L. M. and Rother, K.I. (2014) Challenging Recruitment of Youth with Type 2 Diabetes into Clinical Trials. *Journal of Adolescent Health*, **54**, 247-254. https://doi.org/10.1016/j.jadohealth.2013.08.017

[4] Raynor, H.A., Osterholt, K.M., Hart, C.N., Jelalian, E., Vivier, P. and Wing, R.R. (2009) Evaluation of Active and Passive Recruitment Methods Used in Randomized Controlled Trials Targeting Pediatric Obesity. *International Journal of Pediatric Obesity*, **4**, 224-232. https://doi.org/10.3109/17477160802596189

[5] Schwinn, T., Hopkins, J., Schinke, S.P. and Liu, X. (2017) Using Facebook Ads with Traditional Paper Mailings to Recruit Adolescent Girls for a Clinical Trial. *Addictive Behaviors*, **65**, 207-213. https://doi.org/10.1016/j.addbeh.2016.10.011

[6] Mchenry, J.C., Insel, K.C., Einstein, G.O., Vidrine, A.N., Koerner, K.M. and Morrow, D.G. (2012) Recruitment of Older Adults: Success May Be in the Details. *The Gerontologist*, **55**, 845-853. https://doi.org/10.1093/geront/gns079

[7] Dennis, B.P. and Neese, J.B. (2000) Recruitment and Retention of African American Elders into Community-Based Research: Lessons Learned. *Archives of Psychiatric Nursing*, **14**, 3-11. https://doi.org/10.1016/S0883-9417(00)80003-5

[8] Larson, E. (1994) Exclusion of Certain Groups from Clinical Research. *Image*: *The Journal of Nursing Scholarship*, **26**, 185-190. https://doi.org/10.1111/j.1547-5069.1994.tb00311.x

[9] Otado, J., Kwagyan, J., Edwards, D., Ukaegbu, A., Rockcliffe, F. and Osafo, N. (2015) Culturally Competent Strategies for Recruitment and Retention of African American Populations into Clinical Trials. *Clinical and Translational Science*, **8**, 460-466. https://doi.org/10.1111/cts.12285

[10] Anastasi, J.K., Capili, B., Kim, G.H. and Chung, A. (2005) Clinical Trial Recruitment and Retention of a Vulnerable Population. *Gastroenterology Nursing*, **28**, 463-468. https://doi.org/10.1097/00001610-200511000-00002

[11] Johnson, D.A., Joosten, Y.A., Wilkins, C.H. and Shibao, C.A. (2015) Case Study: Community Engagement and Clinical Trial Success: Outreach to African American Women. *Clinical and Translational Science*, **8**, 388-390. https://doi.org/10.1111/cts.12264

[12] Hurd, T.C., Kaplan, C.D., Cook, E.D., Chilton, J.A., Lytton, J.S., Hawk, E.T. and Jones, L.A. (2017) Building Trust and Diversity in Patient-Centered Oncology Clinical Trials: An Integrated Model. *Clinical Trials*: *Journal of the Society for Clinical Trials*, **14**, 170-179. https://doi.org/10.1177/1740774516688860

[13] Flood-Grady, E., Liu, J., Paige, S.R., Lee, D., Nelson, D.R., Shenkman, E., Hough, D. and Krieger, J.L. (2020) Audience Segmentation as a Strategy for Enhancing the Use of Research Registries for Recruiting Patients into Clinical Trials. *Contemporary Clinical Trials Communications*, **17**, Article ID: 100510. https://doi.org/10.1016/j.conctc.2019.100510

[14] Kost, R.G., Corregano, L.M., Rainer, T., Melendez, C. and Coller, B.S. (2014) A Data-Rich Recruitment Core to Support Translational Clinical Research. *Clinical and*

Translational Science, **8**, 91-99. https://doi.org/10.1111/cts.12240

[15] Lamberti, M.J., Mathias, A., Myles, J.E., Howe, D and Getz, K. (2012) Evaluating the Impact of Patient Recruitment and Retention Practices. *Drug Information Journal*, **46**, 573-580. https://doi.org/10.1177/0092861512453040