Patient Recruitment and Retention

in Clinical Trials

10 Strategies for Success

By forte Research Systems

Introduction

Recruiting and enrolling patients for clinical trials can often be a long and difficult process. It's not surprising then, that finding the target demographic, qualifying and enrolling patients can consume valuable time and money. Therefore, it is imperative that the process of recruiting is well planned and fits within the protocol budget and timeline.

Once patients are enrolled in a study, it can be just as hard to retain them. A variety of unexpected factors can lead patients to withdraw from the study, resulting in inadequate data and potentially, a costlier trial.

This eBook explores common challenges in the recruitment and retention process, and presents 10 keys to successful recruitment and retention that can aid in the success of clinical trials.

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Chapter 1:
Enrollment Planning

Information contained within the *Enrollment Planning* chapter is provided by Jennifer Whitlock, Vice President, Clinical Site Services (CSS).

Jennifer Whitlock is primarily responsible for strategic marketing and product development at CSS. Her team specializes in patient enrollment and retention to helps sites reach their goals. She is particularly passionate about interactive vehicles and social media, leading the digital marketing charge for CSS.

Plan for Success

Before you embark on a patient recruitment campaign, it is important to have a plan. Looking at your available resources, doing your research, and setting goals can help save time and money in the long run.

The best and least expensive patient to enroll into a study comes from the site's own database or practice. These patients already have a relationship with the site, have knowledge of their research, and have been most compliant when participating in research. For this reason, setting the site up for effective internal recruitment through enrollment planning is vital to the success of any study.

Utilize your Own Database

Enrollment planning is a necessity for every study, every time. Consider the following:

- Determine your site's feasibility: Should you even take this study? Every protocol has its challenges, but some are more difficult than others. If your first instinct is one of doubt, then it may be best to pass on the opportunity entirely. Overestimating your site's capabilities and not being able to deliver on it will likely hurt you more in the end.
- It's not always about advertising: Many sites turn to advertising first, without mapping out a plan. Keep in mind, advertising is only one tactic that can be employed when trying to reach your enrollment goals.
- Pick the "lowest hanging fruit:" Reach out to the best qualified and easiest-to-contact potential participants first. You may find great success here, thus minimizing your need to do anything else.
- Exhaust low cost options first: Community outreach, networking and physician referrals are a few examples of low or no-cost recruitment options which your site should first explore.
- Work "inside-out:" Simply put, WORK YOUR DATABASE! Phone calls, emails, postcards, Facebook posts and Twitter tweets should all be a part of your plan of attack for helping to fill your study.

Research Your Participant

Take the time to research and understand the potential participant:

- Who is the ideal participant?

It is best to narrow this down from the inclusion criteria on the protocol. Find out where the peak prevalence/incidence rates are, and let that help guide your decisions.

- What is going to motivate the patient to participate?

There has to be a motivational factor driving someone to consider participation. Is it because someone is seeking new treatment? Or perhaps they don't have health insurance and the medical exams provided at no cost are a benefit for the subject.

- Who is the ideal target?

While most times this is the potential subject himself/herself, there are many studies which require the attendance of a caregiver or family member; an example would be a moderate-to-severe Alzheimer's study. For studies like this, it is important to keep both audiences in mind as you develop your plan and any messaging.

Engage with Sponsors

What do Sponsors and CROs want to see with respect to enrollment planning?

- A written plan, specific to your site: Just the act of putting an actual plan on paper will go a long way in the eyes of a Sponsor or CRO. This demonstrates accountability and a willingness to succeed.
- "Smart" planning: As mentioned previously, exhausting low or no-cost options, in addition to working "inside-out" will be viewed positively. Planning right from the start, even at feasibility, is your best approach.
- Allocation of budget for each tactic: Site recruitment budgets are often incredibly lean. Sponsors and CROs will appreciate you assigning estimated costs to each recruitment tactic.
- Justification for recommendations and costs: Along with costs for each endeavor, it will help to explain why you are making your recommendations. Perhaps you are recommending television; your position will be supported if you mention that television is the most widely used media vehicle in your market against your target audience.
- Metrics, funnel or yield: In simplest terms, "What will this deliver?" Constructing a funnel with an estimated return on a Sponsor's or CRO's investment will demonstrate stewardship over the budget which they have provided to you.

> Sponsors and CROs are becoming increasingly choosy on the sites they initiate on their studies; they want to work with sites that are high performing, enroll efficiently, and are organized with a solid plan of action.
>
> Jennifer Whitlock, Vice President, Clinical Site Services

Assess Results

Thorough enrollment planning would not be complete without measuring your initial plan against your executed campaign and the associated results. Decide up front how you will know which channels worked. How will you know whether it was your TV ad or poster that sent new patients? The Sponsor or CRO would be incredibly interested in a final report, addressing the following key areas:

- What worked? What failed? Why?

Discuss which enrollment tactics worked well, which ones failed, and why they did or did not work. Sometimes you will have answers for why something didn't work well, and sometimes it will not be as clear. Try to arrive at solid answers to justify the results.

- What would you do differently if given the opportunity?

Perhaps the budget was not large enough or the enrollment was highly competitive with multiple sites in a given market area. Whatever the reason, discuss your barriers to recruitment with the Sponsor or CRO.

- What are the bottom line results?

If possible, present your metrics for each recruitment endeavor. Not only will this resonate with the Sponsor or CRO, but this data will be invaluable for your site as you embark on future studies with either similar patient population or similar recruitment tactics.

Chapter 2:
Find the Right Patients

Recruitment Challenges

Adequate patient recruitment is vital for the health and longevity of clinical studies. Poor recruitment can result in loss of patient confidence and loss of revenue. As a result, the site is vulnerable when trying to obtain future trials. However, when done correctly, a successful recruitment campaign can result in lower costs, fewer deviations, and reduced dropout rates.

There are a whole host of reasons it may be difficult to enroll patients, so it is important to know how to address these concerns. The following pages highlight a few common challenges.

According to a study by Tufts Center for the Study of Drug Development, it is estimated that 20% of PIs fail to enroll a single patient and about 30% under-enroll in a given trial.

Misconception about the study

Inaccurate data can significantly affect enrollment. Negative press can almost always be found somewhere – TV, Internet, and even word of mouth. Sites should help potential subjects determine fact versus fiction. Promotional materials should clearly present this information for patients.

According to a 2002 Harris Interactive poll commissioned by The Summit Series on Cancer Trials, 83% of adults believe that clinical trials are essential or very important. However, only 3% of oncology patients in the US enroll in clinical trials.[1] *Therefore, it is imperative that any misconceptions are clarified and the protocol be clearly presented to potential patients.*

Lack of Awareness

Similar to the challenge of misconception comes the challenge of awareness. In one particular survey completed in spring 2000 by Harris Interactive, Inc., 8 out of 10 cancer patients were unaware that clinical trials could be an option for them. This shows the need for investigators and personal physicians to present all possible options to their patients. Increasing awareness of the protocol will have a direct impact on the recruitment process.

There is also a need to increase awareness of clinical trials, in general — not just in regards to the protocol at hand. *One survey showed that 40% of adults do not understand the idea of a clinical trial — what it is or how it is performed. Further, only about one-fourth of the population can even describe a clinical trial.*[3] If the industry works together to better promote and educate about clinical trials, then public recruitment for specific protocols has the potential to increase significantly.

Approximately 69% of non-participation in clinical trials is the result of a lack of awareness the trial is even taking place.[2]

Lack of Access

In addition to creating a positive message and increasing overall awareness, access to the protocol must be made known. Often, patients do not enroll in trials because they have the perception that none exist in their area or for their condition. Perhaps they think that trials are only conducted in large cities and the idea of traveling great distances for care is too much for them to consider. Patients do not often inquire about available trials. Therefore, it is important for physicians and recruiting clinics to do more due diligence when it comes to learning about open trials and sharing the information with their patients. Most patients trust their doctor's recommendations and referrals, and would be more likely consider a trial if their doctor were to discuss it with them.

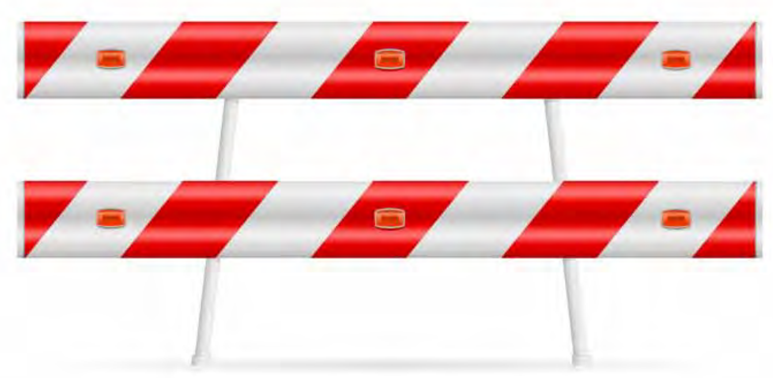
Fear, Distrust, or Suspicions

Many potential subjects are fearful of enrolling in trials because of negative perceptions. Perhaps they are afraid they won't be treated with respect or that they'll be treated like "guinea pigs." Or, perhaps they are fearful of not having control over their treatment. Whatever the reason, it is important to address these concerns when recruiting patients.

Personal Objections

The previous four challenges have all involved psychological factors that can be addressed during the recruitment process. However, dealing with personal objections can be a little more difficult to overcome because of the influence of factors outside your control.

For some, the costs associated with participation and the time away from work are too great. Other times, it may be a deeply rooted personal belief that standard care is better. And yet, in other situations, language or communication barriers exist.



Recruitment Strategies for Success

Many of the challenges associated with poor recruitment can be addressed with the following five strategies. When used collectively, these techniques can boost recruitment numbers, and ultimately, protocol enrollment. They can also aid in successfully completing enrollment timelines.

Later in this book, you'll learn some keys to successful subject retention rates. However, it is important to note now that subject retention begins with the first contact — whether it be a screening call, study visit or advertisement. As you read over the subsequent recruitment tips, consider how you can positively position yourself so that the patient will feel more like a partner in the study and that they are an active participant in their care.

Nearly 80% of clinical trials fail to meet enrollment timelines.[2]

Recruitment Success Tip No. 1:
Know the Target Audience

This may sound simple, but knowing exactly who the protocol is targeting will help you to better refine your recruitment techniques. Rather than targeting everyone, work to segment your patient audience by factors such as age, ethnicity, geography, etc. Then, focus on recruitment techniques that would be best suited to that demographic. For example, if recruiting for a geriatric study, you most likely wouldn't want to promote it online since that demographic is typically not as active on the Internet. Likewise, if it's a pediatric study you probably wouldn't get many patients from hanging posters in a hospital.

> A Pew Research study found that 59% of all American adults are looking up health information online. If you have a target population that has ongoing access to a computer, go online.
>
> Annie Garvey, Director, Patient Outreach, PatientWise

Recruitment Success Tip No. 2:
Consider different Media

Today's technology allows us to reach more people than ever before. Be sure to leverage all media outlets when planning your recruitment initiatives. In addition to traditional methods such as phone calls, chart reviews, TV, and radio, consider all the access the Internet provides. Recruitment can also be done via email, your website, or social media. Though not typically thought of as traditional media, these electronic channels are fast becoming the norm. All these sources can be great places to find future patients for your trials.

What are some other great channels for reaching patients?

- *Direct mailings*
- *Word of mouth*
- *Advocacy groups*
- *Newspaper*
- *Internal databases*
- *Health fairs*
- *Posters at hospitals and clinics*
- *Hospital or Insurance newsletters*

The next page examines some common media outlets and the advantages and disadvantages of each.

> Set up a study-specific landing page or a page of currently enrolling studies to your own website. Since the information has to be IRB-approved, keep it simple – the goal is to get a potential patient 'on the hook' to call or email your site.
>
> Annie Garvey, Director, Patient Outreach, PatientWise

Advertising Medium	Strengths	Weaknesses
Network/Broadcast TV	• Sight, sound, and motion • Highest reach potential of all media types • Immediate reach • Audience selectivity in certain dayparts/ programs	• Highest out-of-pocket costs • Highest production costs • A lot of competition for the audience's attention
Cable TV	• Sight, sound, and motion • Audience selectivity by network • Lower cost than Broadcast TV	• Lower ratings on a per network basis • More cluttered than Broacast TV • Extremely low local reach
Radio	• Efficiency • More segmented audiences - easier targeting • Lower out-of-pocket expenses • Low production costs	• Non-intrusive/background medium • A lot of competition for the audience's attention • Portable medium, not suited for getting an immediate response • More limited reach versus TV
Magazines	• Audience selectivity • Relative efficiency • Allows for complex messaging • Potential for re-exposure through pass-along and shelf life	• Long lead times for space and material • Slow accumulation of audience and reach • Circulation patterns may vary by market
Newspapers	• Builds audience quickly • News environment • Short lead times for space and material • Good for merchandising and promotional support	• High out-of-pocket cost • Relatively inefficient • Cluttered environment • Circulations are in serious decline • Short shelf life
Digital	• Lower cost • Trackable • Numerous advanced targeting options • Good frequency builder	• Slow build up of reach • Some users "tune out" online ads • A lot of competition for the audience's attention

[*] Information in the above table provided by Jennfier Whitlock, Vice President, Clinical Site Services.

Recruitment Success Tip No. 3:
Be Precise

However you promote your study, make sure you are clear and direct in your messaging. Your message should be detailed enough that your target demographic responds, but not so detailed that people exclude themselves before even talking to you.

Ensure that there is a clear call to action for the patient to contact you. Determine if it is best to have them contact you via phone or email. If possible, make the email or phone number memorable. It will make it easier to remember if the patient does not have your contact information directly in front of them when contacting you.

Recruitment Success Tip No. 4:
Be Timely and Responsive

If you choose to have patients contact you via email, there is no need to worry about whether or not you will be at your desk at the exact moment they email. However, if providing a phone number on a radio or TV ad, make sure the clinic is staffed when the ad is aired. Also, if the geographic reach of the recruitment efforts span across more than one time zone, be cognizant that when your office closes at 5:00, it may only be 4:00 in other parts of the country. When patients need to leave voicemails, the risk of losing them dramatically increases. Sites need to follow up with these patients as soon as possible, while the study is still fresh in their minds.

One study showed that sites that waited to follow up with patients experienced a 68% decrease in participation as compared with sites that followed up within one day of referral.[2]

Recruitment Success Tip No. 5:
Measure Results

Always, always, always track your recruitment efforts! By learning what works, what doesn't, and how much was spent, you will be in a better position when starting to recruit for other studies. Carefully and thoughtfully crafted recruitment campaigns can yield terrific results when executed properly. Use these results to show your capabilities and position yourself well with sponsors who may be looking for sites for a new trial.

If your patient recruitment efforts have not yielded the results you anticipated you may need to consider extending the recruitment period, if possible, or looking at new promotional avenues. Be creative!

Chapter 3:
Keys to Retention

Retention Challenges

After spending all your effort recruiting patients, you'll want to make sure they stick around for the life of the study. A multitude of things can occur after enrollment that pose a threat to your retention rates. While some drop outs are unavoidable, there are a number of things you can do to enhance the patient experience and help ensure their completion of the study.

A CenterWatch report stated that dropout rates of 15%-40% are not uncommon, though the average is about 25%.

Reasons for Dropouts

When patients decide they no longer wish to continue with a trial, there are a couple ways they can approach it. They could formally drop out and let the investigator know of their wishes, or they could just "disappear," never showing up for appointments again or returning any communication. Obviously there's not much that can be done for the latter, but when investigators know of a patient's unhappiness, it can provide the opportunity for improvement. Perhaps it was a personal matter for the patient. But, there's also a chance there may have been something else they were unhappy with. Being aware of how the patient is feeling can open up the opportunity to address those concerns, and possibly still keep the patient on the protocol. Or, if the patient's mind has already been made up, you can take their feedback into consideration for future trials and other patients.

Common Reasons for Drop Out:

- Difficulty complying with the protocol – dosages, timelines, or procedures
- AE/SAE
- Loss of motivation
- Peer pressure
- Financial constraints
- Disease improvement or lack of improvement

Retention Success Tip No. 1:
Maintain Communication

Think of a clinical trial as an on-going relationship that needs constant nurturing to grow and succeed. In order to foster this relationship, open, two-way communication needs to be achieved. Patients should have one main point person at the site that they can trust and turn to with any questions. When patients talk to a different person every time or don't see the same people consistently, sites are not able to build as much rapport. Also consider your communication to them — both in form and in frequency. Do you continually share educational materials as they become available? Do you have a newsletter that keeps them informed of activities at the site and various studies? Do you call routinely to remind your patients of upcoming visits? Or, do you call between visits just to ensure their contentment (and hopefully, compliance) with the protocol?

Of course, this consistent communication applies to all study-related information, as new consent forms may become applicable or more educational materials are made available. By communicating all expectations prior to enrolling subjects, the likelihood of them dropping out due to misinformation or misunderstanding decreases.

Retention Success Tip No. 2:
Listen

If you see possible issues arise, be sure to address them immediately. By the time it is brought to your attention, it may already be too late. Therefore, be on the lookout for clues that patients may not be happy or are confused about something. Many times they may not come out and directly say so.

If you do learn of any hesitations, ask the patient to explain further. Listen to what they have to say, be sympathetic, and then figure out the best approach to dealing with their concerns. Perhaps they need more communication from you. Is it possible to reduce their responsibilities at all? Consider any alternative options that would allow them to continue with the study. If they are still not interested in continuing with the study, at the very least, see if they will agree to stay on the study, even if stopping treatment. It may be possible to still use the data. Additionally, you can continue to monitor for any late-showing adverse events. Another way to help monitor patient's satisfaction is to provide a place for confidential feedback or comments. Whether this takes the form of a comment box at your clinic or an anonymous online submission, think of way in which your patients can communicate their concerns, if not in person. It can sometimes be easier for patients to be passive about bringing up some questions.

Every patient is different — standardize the protocol, not the patients.

Retention Success Tip No. 3:
Be Convenient

Since patients are volunteering for the study, try to be as accommodating as possible. Is there ample parking in your lot or nearby? Is your waiting room inviting? Think of how your clinic is presented to the patient. Is it somewhere you would feel comfortable?

Also consider the patient's visit schedule. When possible, accommodate visits around their schedule to increase the likelihood of them keeping appointments and continuing with the protocol. Does your site offer extended or weekend hours to accommodate schedules?

Retention Success Tip No.4:
Maintain a Positive Attitude

In order for your patients to have a positive attitude about the trial, staff need to have a positive attitude. Sometimes when a trial first begins, there can be a lot of excitement built up about it. But, as the trial wears on – especially long-term ones – that excitement can diminish. This can cause everyone to lose interest – including your patients.

Make sure that you keep enthusiasm up and reward success when it's achieved. A happy site can make for happy patients!

Providing positive feedback and encouragement to the patients can also go a long way!

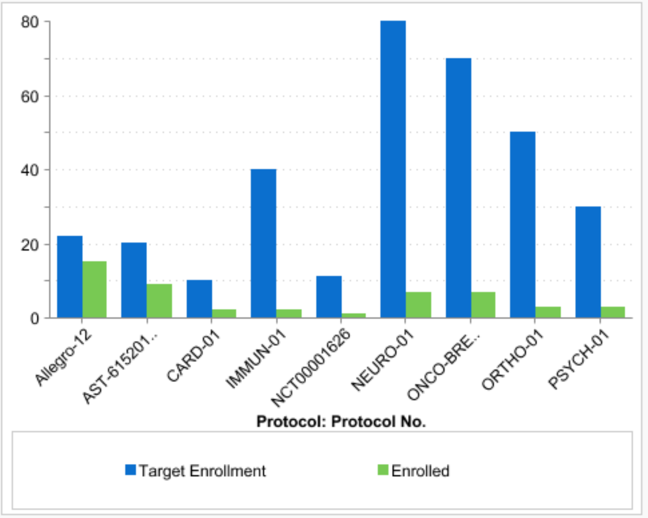
Retention Success Tip No.5:
Know the Protocol

Take the time to ensure that you and your staff are well educated about the protocol. Are there any additional procedures that require further training? If there is additional training that needs to be done, work with your staff to complete it before the study gets underway. Having everyone on the same page and working towards the same goal will create unity within the site, and will show in the way patients view the site and the study.

Chapter 4:
Document Your Work

Track Your Effort

Whether using spreadsheets or a clinical trial management system (CTMS), be sure to always track your effort and monitor your progress. This allows you to make adjustments as necessary and, thus, can save time and money. Find a system for tracking that works for your site — one that allows you some flexibility and is able to track data from start to finish. When the study is complete, it will be helpful to look back at the number of potential patients you reached, how many responded, how many enrolled, how many completed the study, and the costs associated with all of it. Knowing this information from one protocol to the next can help determine budgets and feasibility of future trials.



Using a CTMS

A clinical trial management system is a great tool to manage the day-to-day activities of a research site. In addition to visit management tools, patient databases, and budgeting and financial tools, some also offer functionality to help track recruitment efforts. When you already spend so much time and energy on recruitment initiatives, it can be extremely helpful to have an intuitive system that can auto-calculate costs versus patients contacted or enrolled and can be easily updated as activities occur.

Conclusion

Recruiting can be a long and tedious process, but having a well-thought out plan and optimizing your recruitment efforts can be beneficial from both the time-saving and cost-saving perspectives. With good recruitment efforts, you can acquire some great leads, which with any luck, will turn into some fantastic patients!

Once you've enrolled for your study, you want your patients to have a positive, rewarding experience. By making them feel comfortable, respected, and well informed about the study, you can minimize the risk of drop out.

There is so much more to recruitment and retention than what this book can cover in a few pages. Hopefully, it provides a good foundation for you to build on your recruitment efforts and gets you thinking about new techniques you may not have yet tried.

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About Forte Research Systems, Inc.

We have been providing systems that support excellence in clinical research operations for over a decade. In this time, it has been our good fortune to work collaboratively with our customers as we developed new products and enhanced product functionality to meet the challenges that they face every day. We strive to be the recognized thought leader and preferred provider of innovative solutions that help improve operational efficiency, patient safety, and regulatory compliance.

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