Proactive Patient Recruitment

It's No Longer Novel, It's a Necessity for Trial Success

BY: Melynda Geurts & Dan McDonald

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About this E-book

Patient recruitment is no longer a novel approach to increase the speed and efficiency of clinical trials. Today, proactively planned recruitment programs are common. A decade ago, that was not the case. Usually outside help with recruiting was called upon only after a study was well underway and the study was experiencing enrollment lags. It's more difficult to step in and make a meaningful impact on recruitment after the study is in progress.

In this e-book, we will walk through how things have changed in the world of drug development with regards to sponsor companies and how they see their role in planning and executing clinical trials. We'll share current trends and how those trends are driving a continuous shift from a reactive patient recruitment approach to a proactive one.

Also included is data from a survey conducted by Imperial to look at the perspectives of patients when it comes to the awareness of clinical research and how they learn about clinical trials. Finally, we present a case study demonstrating the differences between reactive and proactive recruitment strategies.

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Table of Contents

Introduction

Our many years of experience in patient recruitment have been a fascinating, and at times frustrating, journey—often at the same time! One important aspect has changed: few sites and studies can meet enrollment targets without some type of external support.

External support means more than traditional advertising—it now runs the gamut of different means to reach potential subjects, including digital marketing, websites, social media, apps, and site support.

Today's modern environment requires targeted patient recruitment and engagement for clinical trials to succeed.

Chapter 1:
The World in Which We Live

Science and technological innovation have significantly advanced the benchmarks which must be achieved in clinical research to bring new therapies to market. While this advancement allows pharmaceutical and biotech companies to bring new compounds into the pipeline, it also increases the burden of conducting clinical trials.

Clinical trials involve five main groups, each with different views, experiences, and motivations. Here is what they are saying about clinical trials[1]:

In combination with these stakeholders, there is a multitude of service providers that come into play at different points along the way. All of these organizations have a different role in the successful enrollment of the study. In order to provide the resources, the knowledge, and the support necessary to be successful, some of the realities related to each of the stakeholders should be examined.

When it comes to sponsors, 70 percent report that the hardest part of patient recruitment is finding the right investigators. So often, sponsors are focused on getting that particular component right. When they don't, traditionally the response has been to simply add more sites to the mix. Outcomes of this approach are inconsistent, but it is still frequently used today. But there are realities from a cost perspective that need to be considered.

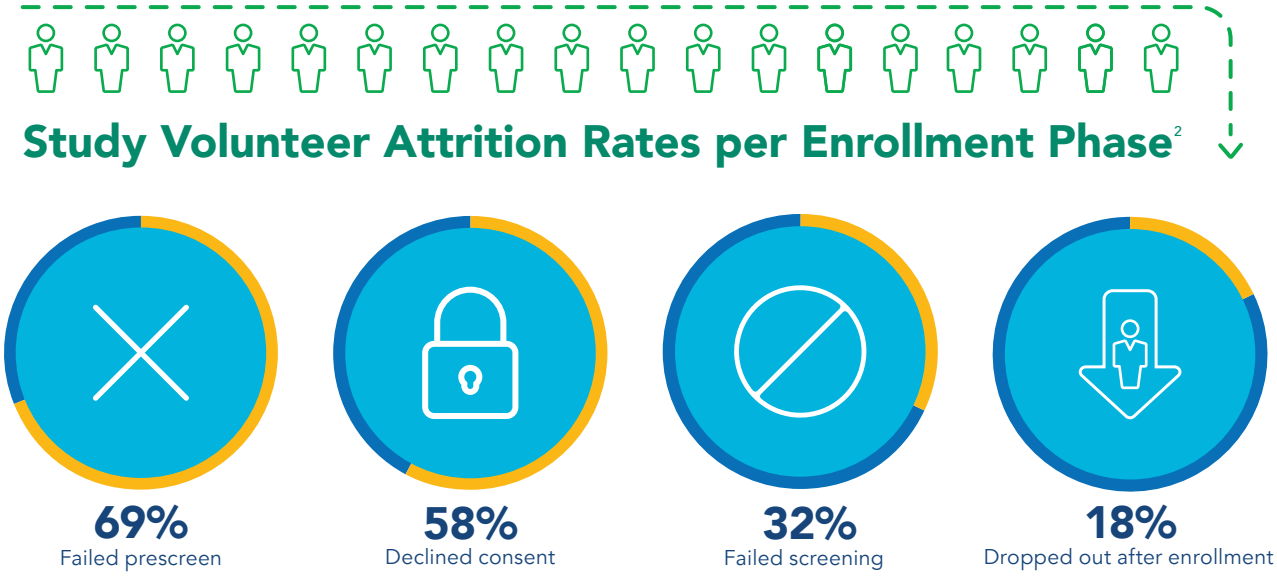
When it comes to the patient's viewpoint, 69 percent said they have not participated in clinical trials because they were not made aware of any trials.

1 ClinicalTrials.gov, Tufts, ISR Reports data

Awareness is a huge factor in successful enrollment. We recently attended a conference in Philadelphia called "Patients as Partners." For the first time in our 20 years in the industry, there was a formal gathering of these different stakeholder groups to discuss the critical role that patients play in the success of a study.

There was a large number of patients at the conference who shared their perspectives on studies. They talked about how they learned about studies and what their experiences were like. Much of what they said pointed to lack of awareness and education throughout the process.

For patients who are interested and do volunteer, far too many still don't qualify for the study or stay or they leave the study after they are enrolled. Here is data from CenterWatch that illustrates this trend.



Why are these metrics meaningful?

When planning a protocol, there are questions you need to ask yourself. Am I looking from and understanding the patients' perspective with this protocol? Does my protocol take into consideration whether these types of patients really exist? Are the obligations and requirements of the patient fair? Often the protocol is first and the patient is second when it comes to protocol design. This orientation lends itself to the statistics above.

2 CenterWatch 2014-2015 Clinical Trials Data Library

The next graphic presents additional considerations to take into account during the protocol design process and also in any communications with the patient.

Reasons Patients Failed To Complete a Trial[2]

25% Side effects/Adverse reactions

21% Change in medical situation precluded participation

8% Insufficient/No compensation

8% Not comfortable with study/meds

8% Treatment ineffective

Note: 30% of survey respondents did not reply to this question

By addressing these specific issues early on, it will be easier to establish realistic expectations on the patient's part before they join the study, and it will limit them as reasons for attrition.

Protocol crowdsourcing has been growing in popularity. This, along with other new market research methods and focus group surveys, are bringing protocols to the patient early to get a patient perspective on components of the protocol. When prospective patients are able to provide feedback around items, such as informed consent, site-visit requirements, procedures, and more, useful proactive adjustments can be made to protocols.

It is also vital to consider the caregiver requirements if they will be helping a patient participating in the study. For example, with the increase in the number of Alzheimer's and oncology studies, more caregivers are playing a critical role in the retention and compliance of patients.

Chapter 2:
The Shifting Landscape

Some of the most significant shifts in clinical trials today are the result of technological developments. These changes promise to have a dramatic impact in the way patients are recruited and kept engaged in studies.

Wearables like the Fitbit and the Apple Watch are making strong headways in the commercial arena for individuals to monitor their health. However, it is not known how they will find a role in clinical trials. Apple's ResearchKit captures real-world, qualitative data. How should tools like this be integrated into protocols? Can they improve the drug development timeline? This can be done in a number of ways, such as improving patient engagement, but also by allowing for more decentralized research.

Participation is moving away from the study site. In our mobile world, study research is being taken to the patient's home, their place of work, and also to their primary care physician's office. As technology continues to improve and increase its reach, so too will decentralization.

While the thrill of a new smartphone excites many of us, technology and our health are a relatively new relationship. Giving researchers access to our vitals 24/7 can be off-putting. Sharing personal ailments via social media can be uncomfortable. A lot of technology in health care is in its infancy stages with low adoption rates. How quickly that will change is an ongoing question.

Another significant landscape shift falls into the regulatory category: the role of payers. Payers are becoming more scrutinous around the reimbursement of medications, medical treatments, and procedures.

These changes can have a real impact on the enrollment of studies. Payers are now looking closely at value-based metrics and are increasingly pushing sponsors to conduct trials in real-world populations. These include older populations, ones with poor health and comorbidities, different ethnic populations, different age groups, and populations with a varying genetic makeup. This is a reality of research today that is driving an increased burden on study staff and other supporting trial resources. It often lends to extended timelines.

Chapter 3:

Keeping Pace: Listening to Our Audience[3]

30% caregiver to a person with condition

70% live with a condition

20% Men
80% Women

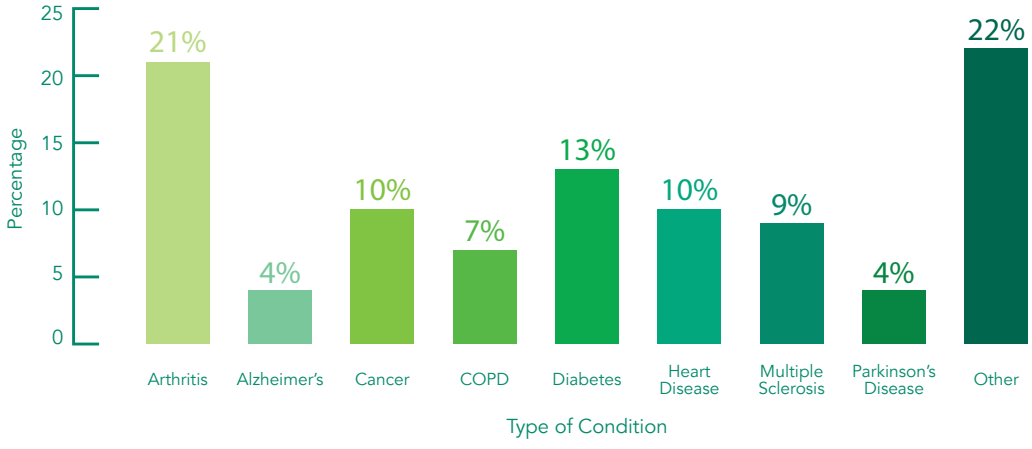
5% Ages 18-34
32% Ages 35-54
33% Ages 55-64
30% Ages 65+

3% Hispanic
4% Black
7% Other
86% White

Last year we conducted a survey targeted toward patients and caregivers with the objective of gleaning insight on several key topics. They were questioned about how they gather health care information, make decisions, and how they are using technology to advance their understanding or decision-making when it comes to health care.

More than 4,500 responses were collected over a two-month period. The demographics were as anticipated based on other similar surveys.

Conditions Affecting Those Surveyed[3]



3 Health Care Decision Survey 2016, Imperial

The largest therapeutic condition grouping fell into the arthritis category at 21 percent, followed by diabetes at 13 percent. The remainder includes cancer, multiple sclerosis, and heart disease, each falling around the 10% range.

Where are they seeking information?[3] It's interesting to take note of the two leading information channels represented: health care providers at 79 percent, then the Internet close behind at 72 percent.

Use of the Internet as a resource will likely increase. Through conducting focus groups, along with other patient-centric activities, we have found that newly-diagnosed individuals will often go to the Internet first for their research. They want to learn everything and anything they can about their recent diagnosis. In some circumstances, this is a positive event where the information removes some level of uncertainty, gives back control, and settles their anxiety. Other times it only compounds the fear for the individual and any associated caretakers. The issue at hand is the Internet is a large ungoverned body of information where the best explanation, or the truth for that matter, is lacking. Almost all cases in our research found regardless of what the patient learned from the Internet, they would speak with their primary physician about options and next steps.

We are often asked if the U.S. National Institutes of Health's website, ClinicalTrials.gov, is effective in patient recruitment. It has helped increase awareness about studies, but it should not be considered a stand-alone recruitment tool.

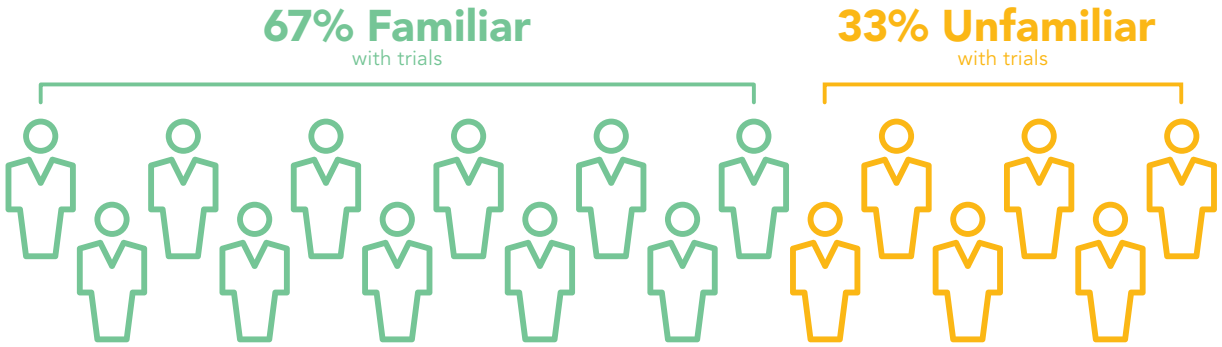
ClinicalTrials.gov is somewhat tedious in terms of navigating. Much of the content is not very patient-friendly, and it can be confusing. Sponsors should look at other online clinical trial listing services and registries, or even develop their own trial website and do marketing around that. When patients visit a website dedicated to a specific study, they will find content created to be relevant to them, with messaging that will resonate with them, and hopefully get them to take action and ask for more information.

3 Health Care Decision Survey 2016, Imperial

We recently had the opportunity to be part of a series of focus groups for men who were diagnosed with high-risk prostate cancer and to share with them some study-specific materials related to a trial. They were asked how they went about learning more about their disease once they were diagnosed. Resoundingly, each had immediately jumped on the Internet to find information.

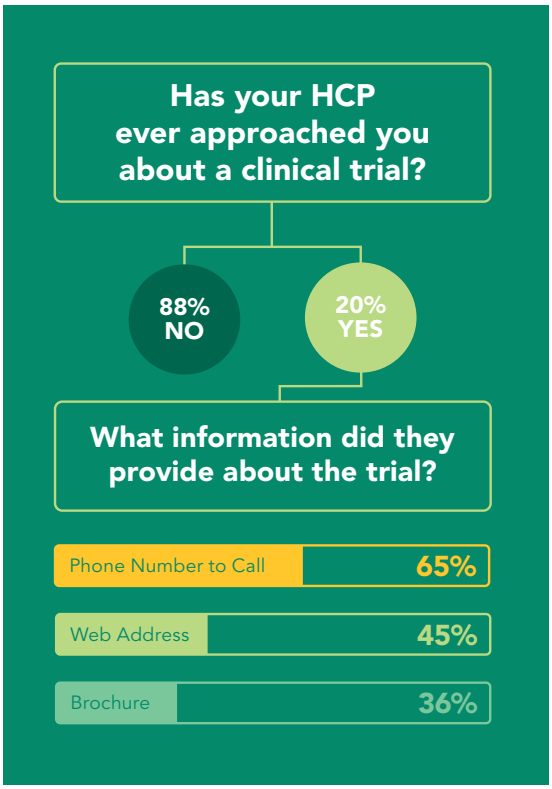
Half of the participants told us that when they saw the URL ClinicalTrials.gov within the materials, it gave that study more credibility. A study-specific website is a more appropriate way to get quality referrals, and be able to track and determine ROI for a program you put in place. However, any way you can tie in the ClinicalTrials.gov website, it is worthwhile. From a patient's perspective, it puts a stamp of credibility on your trial.

Ultimately, the onus is on the drug makers to get the appropriate education about clinical trials being conducted into the hands of referring physicians and health care providers. This continues to be a problem area for the industry.



Well over half of our respondents, 67 percent[3], said they were familiar with clinical trials. If you have been fortunate enough to hear Ken Getz, director of sponsored-research programs at Tufts Center for the Study of Drug Development, speak on this topic, you will know that he says awareness is high, but participation is low in those who have not done a trial previously. The issue at hand is how to effectively message and educate people about trials in such a manner that it encourages engagement.

3 Health Care Decision Survey 2016, Imperial



Primary care physicians are often trusted resources, and they have the ability to educate as well as direct their patients to studies. However 88 percent of our respondents told us their provider had never mentioned or referred them to a study.

This shows a lack of awareness of the issue among the medical community as well. Awareness requires constant education and messaging about trials being conducted in health care providers' areas, which includes helping sites connect with physicians.

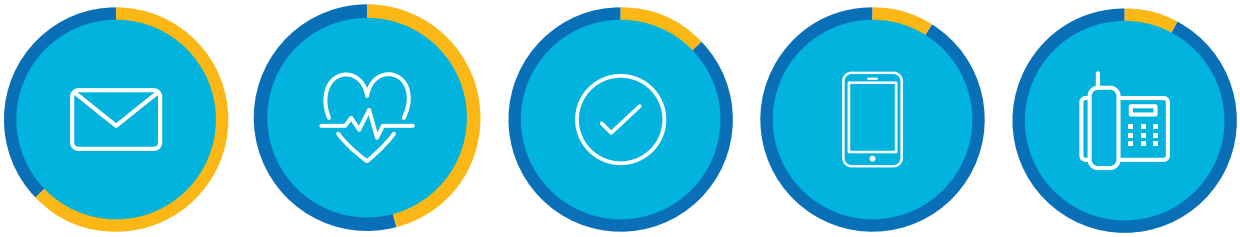
The numbers shown in the graph below represent lost progress and opportunity, especially when 42 percent said they would consider participating in a trial. Of those interested in participating, 32 percent said it would be to help with their current ailment. We believe that predominantly these are individuals already receiving some level of treatment that they are unsatisfied with or are finding ineffective. Gaining knowledge, helping to find a cure, and paying it forward to future generations were additional reasons given.

Why 42% of People Would Consider Participating[3]

Note: 10% had no response to this question

3 Health Care Decision Survey 2016, Imperial

How They Prefer to Receive Information[3]



63% Email Notifications

46% Their Doctor

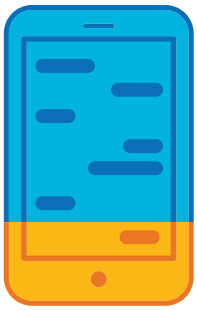
13% All of the Above

9% Text Notifications

8% Phone Calls

In our survey, respondents were asked how they prefer to receive clinical trial information, and 63 percent said via email. About half, 46 percent, still preferred face-to-face communications with their doctors, 9 percent preferred text notification, and not far behind is 8 percent by telephone.

Use Text Messaging[3]



73% YES

27% NO

Use Health-Related Apps[3]

32% YES

68% NO

In an era ruled by smartphones, it is not surprising that 73 percent of respondents said they use text messaging. Mobile technology has opened up significant new pathways to connect and engage with patients. Not only through text messaging but also through mobile applications.

However, while it's challenging to find someone not using Facebook, Twitter, or Instagram during their day, when asked if they use health-related apps, 68 percent of those surveyed said no. There can be a comfort obstacle with putting personal information into an app, and quite frankly, people don't yet associate their smart devices with their health.

Surveys such as this one can lend valuable insight to study development. Recently we have been working with sponsors

3 Health Care Decision Survey 2016, Imperial

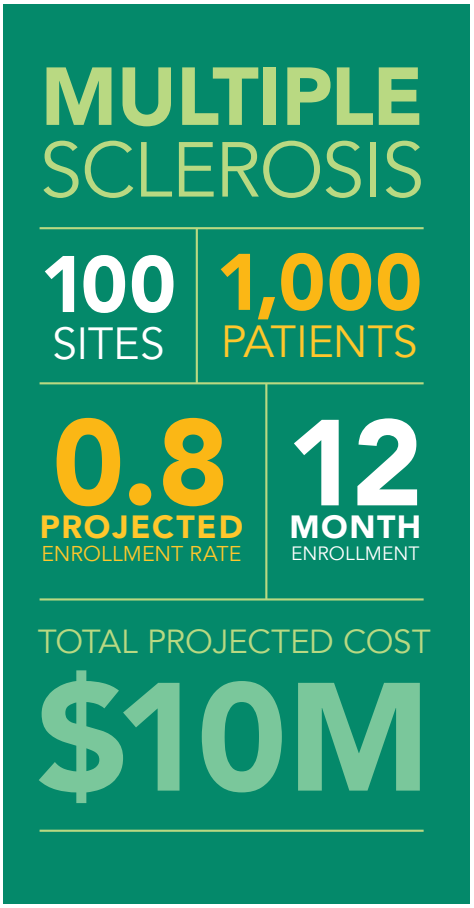
in organizing focus groups and social listening initiatives. These have been powerful tools for engaging patients through additional mediums. It is best to gather patient perspectives from as many channels as are available to you.

With regards to patient recruitment in emerging markets, a more traditional approach is called for. This requires a heavy reliance on the medical community and the patient's physician to raise awareness about the trial and make a recommendation for enrollment. That's good and bad, depending on how you look at it. It could create a roadblock if the physician is unwilling or is frankly just unknowledgeable about clinical trials that are taking place in his or her area. It could also be a benefit if that physician were to ultimately refer a patient. Based on our experience, the patient is typically better qualified to participate in the trial, because they've had that medical vetting by their physician.

But changes are expected in some countries. In recent years, especially the last two, patients have been getting more progressive in terms of going outside of their health care provider to learn about options. They get involved with patient association groups, which are the equivalent of our support groups or patient advocacy groups.

Chapter 4:

The Importance of Planning: A Case Study



If you have a lot of sites dropping from your study, and you're having to replace those sites, there's obviously an associated cost. Those costs, and changes from protocol amendments, can have a huge impact on your overall budget.

Site attrition can accrue into a significant cost burden and negatively impact your budget. Consider this case study: This study was a multiple sclerosis program with 100 sites and 1,000 patients. The projected rate of enrollment was 0.8 patients per site, per month, over a 12-month period. The total project cost was budgeted at $10 million.

Option 1: Amend the Protocol (Reactive)

You've received feedback from sites, and they are letting you know that they believe the best way to impact enrollment is to amend the protocol. Amending the protocol averages about a million dollars.

Then a decision is made to replace 30 low-performing sites. The average cost in the U.S. to replace a site ranges anywhere from $30,000 to $40,000.

Replacing 30 sites at $30,000 adds $900,000. You now have a total amended project cost of $11.9 million, which is a 19 percent budget increase.

Amend Protocol = $1,000,000
Replace 30 low–performing sites: $900,000
Total amended project cost: $11.9M
19% budget increase

Option 2: Add a Centralized Recruitment Campaign (Reactive)

Let's consider a second option. This is another rescue situation, but the sponsor has decided to add a centralized recruitment campaign. There is a startup timeline of about 2-3 months with a cost of $250,000 to get the program implemented. With a recruitment campaign to support this study and get it back on track, it's going to be about a million dollars.

Now you're looking at a total amended project cost of $11.3 million. It's still a 13 percent budget increase, but a little bit less than option number one provides.

Addition of centralized recruitment campaign
Startup timeline of 2–3 months: $250,000
Recruitment campaign: $1,000,000
Total amended project cost: $11.3M
13% budget increase

Option 3: Implement a Proactive Recruitment Program

Now let's look at this from the proactive perspective, still using the same study example. Before the study starts the sponsor decides that it will proactively factor in a recruitment program. That recruitment program is going to cost $500,000. That figure represents the only additional cost that they need to add to the project budget. Now you have a total amended project budget of $10.5 million, which is a 5 percent budget increase versus a 19 or 13 percent budget increase.

Implement a proactive recruitment program: $500K
Total amended project cost: $10.5M
5% budget increase

There can be a tremendous cost savings by planning proactively. Plan for the what-ifs. More and more sites and sponsors are putting a recruitment services line item in their study budget. That says a lot about where we are in this industry, and where this niche is, from a planning perspective. That is important. Even if you don't need

to implement the program, you have it budgeted. You can have it developed, and it can become an immediately available turnkey option.

About 60 percent of the programs we see are from a proactive perspective. Sponsors know up front that there be inherent challenges to the way the protocol is designed and to the way that they will have to execute the study at the site level. They've taken the time to understand the patient perspective and the caregiver perspective, and factor that into the type of support that the study requires to be successful.

One area where proactive work is occurring is oncology. Proactive work is occurring in oncology because the competition has grown so fierce that companies have to be more aggressive in their educational efforts.

The mindset in these organizations is evolving. They're increasingly understanding that patient recruitment should be largely focused on education and awareness-building within the patient population. Creating a sense of comfort in the patient's mind about how they'll be taken care of in the study and the efforts being made to make their continued participation easier is important.

The final piece is the role that the medical community plays in raising awareness about the study and encouraging referrals. Typically there's a lot of work involved with such programs and the yield is usually lower than, for example, a direct to patient advertising campaign. But they can often be critical in driving enrollment results in oncology trials. That's just one of the areas where a shift is occurring in the trend on terms of proactive versus reactive.

Chapter 5:
The Site Role in Patient Recruitment

Increasingly, sites, especially fulltime clinical research sites, have become more formal in the way they approach their obligation to enrollment. Sites are adding staff members dedicated to patient recruitment, and study coordinators are much more well-versed in the world of patient recruitment. There's a lot of information available right now in terms of industry publications, including e-books like this one.

One way to engage sites and get their buy-in about patient recruitment is by engaging them early and asking for feedback often through surveys and interviews. Ask about the strategies that have worked for them and what they have done in a similar studies in the past that were effective. Also, what type of support would they like to receive from the sponsor company? If you ultimately decide to implement centralized recruitment programs, those sites have a higher rate of adoption, and use of those programs, if indeed you got their buy-in at the beginning.

You might have heard the ratio of a third, a third, a third. A third of the sites are going to meet and exceed their enrollment goals, a third will just meet their goals, and a third of the sites typically don't even get one patient enrolled into the study.

It's natural to want to be fair and support all of the sites that are participating in your program. But there comes a time to evaluate the sites. You will find that some are better structured to take advantage of the additional support services and materials that you're able to provide. Devote resources to them to help get the study completed on time.

About the Authors

Melynda Geurts, M.S.

Vice President of Operations
Imperial Patient Recruitment and Engagement Group

Melynda is a 22-year clinical research veteran with expertise that spans protocol planning, recruitment, retention, global regulations, emerging markets, and more. Melynda is a 2008 inductee into *PharmaVoice* magazine's 100 Most Inspiring People in the Life Sciences. She has written extensively for clinical trial trade publications and blogs at ImperialCRS.com/blog. She is author of the e-book *Tricks of the Trade: Recruitment and Retention Planning for Different Study Types* and is co-author of the e-book *Your Patients Are Here: Where to Recruit & How to Retain Highly Engaged Patients.* Find these and other books of hers at www.imperialcrs.com/resources/ebooks.

Dan McDonald, B.S.

Director of Business Development
Imperial Clinical Research Services

Dan is a seasoned clinical research executive with more than 17 years of experience supporting biopharmaceutical companies with the planning and execution of their pivotal trials. Dan serves as director of business development, working from Imperial's Boston offices to identify opportunities, build strategic partnerships, and manage contract negotiations. He has written for many industry publications, is a popular conference presenter, and has conducted numerous workshops on patient recruitment for clinical trials. He is co-author of the e-book *How to Turn Around a Slow-Enrolling Trial* and he also blogs at ImperialCRS.com/blog.

If you have questions about patient engagement and how to increase enrollment into your trials, we would love to hear from you.

Melynda Geurts
mgeurts@imperialcrs.com
469-916-8636

Dan McDonald
dmcdonald@imperialcrs.com
508-342-5315

Connect with us on: