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22 The Michael J. Fox Foundation on Overcoming Recruitment Challenges
Accelerating Drug Development for the Field: Building Clinical Trial Recruitment Infrastructure in Parkinson’s

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There is no “department of cures.” There are many diverse players involved in drug development, each of whom brings critical financial, intellectual, and human resources to the process. However, no one is in charge of the overall direction the field takes—charting the course and addressing challenges as they arise.

Recognizing this, the Michael J. Fox Foundation (MJFF) for Parkinson’s Research endeavors to play this role for Parkinson’s disease (PD), a progressive neurodegenerative condition characterized by slowness in movement, gait problems, rigidity, and tremors. The foundation's singular focus is to develop new therapies and, eventually, a cure for this condition.

As the world’s largest nonprofit supporter of Parkinson’s research, MJFF has funded more than $450 million to date to bridge the translational research gap. The foundation combines this funding with intellectual resources, person power, a venue for collaboration, and leadership of the field to objectively address key roadblocks in drug development for PD.

Although the research the foundation has funded to date is a critical contributor to its impact, the thought leadership, staff-directed activities, and collaborative discussions it facilitates are also vital in accelerating the course of drug development in PD. MJFF is constantly scanning the PD landscape to determine systemic trouble spots for the field and, where it is clear that the foundation can play a role, quickly deploying resources to address them.

Focus on Trial Recruitment

Clinical trial recruitment emerged as a priority over the last three to five years, as the understanding of the underlying biology and genetics of PD increased dramatically. These new findings have spurred more activity than ever before to develop new therapies to improve PD symptoms and to slow or stop the progression of the disease. Consequently, treatments aimed at new targets are moving swiftly through the drug development pipeline and beginning to enter clinical testing.

Seeing this unprecedented activity approaching the clinic, the foundation acknowledged an opportunity to enhance the PD risk profile to make it more attractive for industry to test promising compounds. MJFF has since prioritized opportunities to identify strategies to decrease the time and cost it takes to conduct a trial.

Like trials in most other disease states, PD trials are chronically slow to recruit. Across central nervous system (CNS) disease trials, there is an average 116% increase in the enrollment timeline to fully recruit a study—more than double the timeline set at the study start.

About 37% of sites in a CNS trial underenroll, which increases the recruitment burden of high-performing sites and often requires unplanned time and investment to activate new sites. The average enrollment rate in CNS studies averages .85 subjects per site per month. Also, the costs associated with recruitment, not to mention extended recruitment timelines, are staggering. Anecdotally, sponsors budget $3,000 to $10,000 per enrolled subject for recruitment alone.

Thus, recruitment is one of the most costly and time-consuming aspects of testing compounds in humans. This, combined with the unique patient and research community constituents we work with, makes trial recruitment a prime opportunity for focus.

This article addresses the challenge of clinical trial recruitment in PD, describes patient and site/
sponsors strategies that the foundation has implemented, and shares outcomes on the progress of these efforts to date. Although the learnings, examples, and outcomes provided here are all specific to MJFF’s experience, many lessons are likely applicable to other organizations and diseases.

**Why is Participation in Trials So Poor?**

The foundation’s due diligence to date on recruitment targeted three key stakeholders in the trial enterprise—the patient community, trial sites, and study sponsors—and identified key challenges and deficiencies in each group to inform programmatic design.

**PATIENT COMMUNITY**

Successful clinical testing of a new therapy requires patients to play a role that no one else can play. No matter how many dollars, brilliant researchers, hours, and goodwill go into planning a trial, there comes a moment when the sites are activated, the clinic doors open, and patients are literally the only players who can move things forward.

In 2011, MJFF began due diligence with an informal survey of 832 patients to better understand their knowledge of trials and their perceptions about them. The results indicated that less than one in 10 PD patients had participated in a trial, although more than 80% of respondents were at least “somewhat likely” to be willing to participate in one.

In exploring this further, three key needs in the patient community emerged: awareness building about the need for people to participate, education about what a trial entails, and an easy action step to actually find a trial in which to participate.

The survey shed light on the need for awareness: 39% of respondents in the survey stated that “clinical trials for Parkinson’s have little trouble recruiting volunteers.” Patients will only know that trial participation is possible when they are aware that a trial is happening and recruiting volunteers.

Clearly, knowledge is lacking within the patient community that trials struggle to recruit, and this key underlying principle must be communicated widely. Such a lack of awareness may stem from the fact that clinical trials are not part of the standard dialogue between a patient and treating physician. This is especially true if the treating physician is not also conducting research, which makes it even less likely that the physician will integrate discussion of trial participation into a patient’s visit.

Once patients are aware they are needed, education on what it means to participate is important. The survey findings included the following:

- 46% of respondents stated they believed it was true that patients in clinical trials are “guinea pigs”
- 32% believed that participating in a trial meant exposure to experiments to which they did not agree
- 33% stated that participation in a trial would interfere with their usual care

Such common misconceptions must be addressed and demystified to increase willingness and convert awareness into active trial participation for most people.

Once aware and “primed” through broad education about what is involved in trial participation, the final, and perhaps most important, step is providing an easy action item that people can follow to find out about specific trial opportunities that are a good fit for them on an ongoing basis.

As the world’s largest nonprofit supporter of Parkinson’s research, MJFF has funded more than $450 million to date to bridge the translational research gap.
The resource most often cited to find trials across all diseases is ClinicalTrials.gov. Although this is a useful tool for select purposes, and one many patients use to find trials, it has several shortcomings, making it ill-equipped to serve this specific purpose: The language used on the site is very scientific; searches cannot be tailored to a patient’s profile; and recurring alerts about new trials are not possible. ClinicalTrials.gov is an immense resource, but it was simply not built to serve as a recruitment portal or to be a resource for the general public.

Better solutions must be developed to better meet the patient community’s need to access information about currently recruiting trials for which individuals might qualify.

**TRIAL SITES AND STUDY SPONSORS**

Of course, patients are just one part of the equation. They have to have somewhere to go, and they need the system and processes set up to receive and enroll them into a study. Sites and sponsors play an equally important role in addressing this challenge in the trial ecosystem.

Sites are faced with many barriers to recruitment, some involving logistical and operations hurdles, and others in the realm of strategy and core skills. At its very foundation, clinical trial recruitment is a sales and marketing activity. Often, and importantly so, site teams working on a study have science and medical training. However, at the recruitment stage of a trial, strategic marketing, planning, and sales tactic implementation are needed most.

Additionally, sites tend to have a standard approach to recruitment for all trials. Tagging charts and recruiting from an investigator’s panel of patients is the classic recruitment plan for a site starting a trial. Some sites may have plans for outreach to their physician colleagues, speaking at support groups, or center newsletters as part of their standard study start plans, as well. Rarely, though, is the recruitment plan for a study tailored to the “target patient” a study plans to recruit. Even more infrequently is a plan mapped out by a site pronto study start. Such factors make it difficult for sites to budget for and justify funding for novel tailored strategies appropriately.

In this environment, study sponsors also play a critical role. On the one hand, recruitment is a prime expense and concern; on the other, sponsors leave much of this up to the sites. In the typical multisite study, a sponsor may provide recruitment materials and some funding for advertising, but otherwise does not spearhead the development of a tailored recruitment plan or work with individual sites to determine how best to implement it locally.

The kind of resources and support sponsors provide plays a significant role in the trial recruitment ecosystem, often leaving sites underfunded and ill-supported to execute on strategies that will be most fruitful for their study.

**Addressing Slow Trial Recruitment Throughout the Field**

MJFF identified the easy-to-use action step for patients to connect to trials as the first critical need in addressing slow recruitment. Aiming to leverage advancements in technology to facilitate expedited recruitment, the foundation created Fox Trial Finder, a web tool that matches PD patients and control volunteers to research teams running open clinical trials.

Here is how it works: PD patients and control volunteers visit www.foxtrialfinder.org to save a profile that includes their age, gender, location, date of diagnosis, disease progression, symptoms, treatment history, and knowledge of genetic mutations associated with PD. Simultaneously, the coordinators of trials that have been approved by the appropriate institutional review boards are invited to submit descriptions of their studies and the profile of the ideal subject they are looking for, based on study inclusion/exclusion criteria.

Volunteers and trial teams are matched to one another through the website’s proprietary algorithm, which takes into account an individual’s profile and the profile of the volunteer that each study is looking for.
Clinical trial recruitment emerged as a priority over the last three to five years, as the understanding of the underlying biology and genetics of PD increased dramatically.

Launching in beta in July 2011 and officially in April 2012, Fox Trial Finder has amassed a database of more than 28,000 interested volunteers to date, and lists between 280 and 320 actively recruiting trials at any one time. Figure 1 indicates the growth in volunteer registrations through November 2013.

As of June 6, 2013, 466,979 matches had been generated between potential participants and recruiting trials, and 16,694 messages had been sent between interested potential participants and trial teams. A survey sent out to the database indicated that 38% of respondents have inquired about a specific trial and 11% have enrolled in a clinical trial using Fox Trial Finder.

Trial teams using Fox Trial Finder as a recruitment tool report accelerated recruitment timelines. From the patient perspective, Fox Trial Finder is a “one-stop shop” to learn about PD trials they may qualify for that are currently recruiting or are soon to begin recruiting, and to identify and connect with sites in their area that are recruiting subjects.

**What More is Needed?**

Launching Fox Trial Finder is not a complete solution. It might suffice for the first 10,000 to 15,000 volunteers, but for most of the 5 million PD patients worldwide, more is needed.

Since the launch, staff activities have focused on awareness building and education about the need for trial participants, beginning with our own e-mails, blog, newsletters, social media, and events. These foundation communications have focused on the need for recruiting volunteers, demystifying key myths about study participation, and sharing profiles of study volunteers with others. Also, a group of more than 150 Fox Trial Finder ambassadors has formed to empower champions of the site to make presentations and disseminate information about it.

Next, an extensive suite of materials was created to support outreach initiated by the foundation, patient ambassadors, trial sites, and others. Additionally, a new event series called Clinical Trial Fairs has been launched, bringing the concept of job fairs to clinical trials by inviting patients to browse tables hosted by local sites and adding an education symposium to demystify what is involved, what regulatory protections exist, what the consent process entails, and more.

From the three fairs that occurred in San Francisco, New York City, and Chicago, trial sites left the fairs with a combined 1,059 people to contact about participating in their studies (see Table 1 for additional details). Finally, a partnership among 16 other regional, national, and international PD organizations was formed to raise awareness about the need for participants and to educate about trial participation. Importantly, this group has agreed to share one consistent message and suite of materials about trial participation, driving people to Fox Trial Finder as a next step.

All of this is contributing to an ever-growing mass of volunteers who are educated about participation, well characterized in a database, and who can be relied upon by the field over time to participate in studies.
Of course, Fox Trial Finder only facilitates matching people to trials; actually enrolling them requires much more, including many offline activities funded, planned, and initiated by study sites and sponsors. Acknowledging the need to address this issue from all sides, the foundation also built a new team to support these key stakeholders in their recruitment activities.

The signature program of the site- and sponsor-oriented activities is recruitment planning support provided to all foundation-funded and sponsored studies. This offering requires all of the foundation's awardees to plan for recruitment as they are applying for funding, to work with the team to refine their plan and budget accordingly upon study initiation, and to participate in regular recruitment update calls throughout the life of their grant.

Over time, these activities have enabled the foundation not only to help the actual studies with which it is working, but to become a long-term resource for recruitment knowhow in the PD field. This makes it possible for the next study trying to recruit a specific target or include a nontraditional procedure to leverage the lessons learned from a past study that faced a similar challenge.

Lessons Learned

From these activities, many key insights have emerged. First, planning ahead works. As evidenced by the decrease in the number of studies that have required "rescue" strategies, thoughtfulness about tactics and budgeting up front for recruitment plans have benefited recruitment timelines. Tailored, multipronged, phased strategies also seem to be the most successful. Working with sites to think hard about where they are going to find their target patient and sharing lessons learned from other trials have been most helpful.

Also, ensuring several tiers of plans has equipped trial managers with a long list of quality approaches to pilot and expand (or pilot and discontinue), depending on how well they work. Marketing assistance has helped study leaders think about crafting materials to inform patients about studies and cultivate them along the way.

Many studies provide an entire list of inclusion/exclusion criteria on recruitment materials, which can be overwhelming for patients. Others fail to explain the goal and scientific rationale for the study, skipping over information of primary interest to potential subjects and oftentimes the key motivator for participation. Information about a trial opportunity must be provided in a clear and concise manner, and patients need to understand trial goals and requirements for participation.

Helping the research team think about how to present complicated science simply and reformulate study communications has been beneficial. Finally, working with sites on strategies to convert qualified leads has been important. The leaky pipe metaphor highlights the role a site and sponsor can play in identifying "leaks" (i.e., why and where a subject will opt out of the enrollment process).3

Addressing issues related to the logistics and activities of a trial that could be valid reasons a subject may decline participation is a key recruitment planning activity that is often overlooked in planning, and sometimes ignored even once the trial is under way. Factors such as transportation, time required for participation, and reimbursement are valid and real day-to-day concerns for potential trial volunteers. Ensuring that trials have an adequate budget to provide parking or transportation service, have flexible operating hours, and can provide some reimbursement for patient time are simple fixes to these types of "leaks."

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*Due to the recency of these events, numbers provided only represent data collected to date. Contact the lead author for updated numbers.
Other conversion issues may arise due to a daunting or difficult procedure included in a trial. In one ongoing study requiring seven spinal taps, significant planning and site support were provided to address this procedure: Principal investigator and coordinator talking points were developed; observation of the procedure with experienced colleagues was planned for; and a patient handout and video were created to explain the procedure. Although most sites had an early learning curve, all of them became experts at speaking to patients about this, so much so that the spinal tap is almost never cited as a reason for turning down enrollment in the study. Further, continued willingness to complete this procedure has sustained, with more than 90% of sites that were expected to involve a spinal tap being successfully completed.5

Resources and Further Considerations

MJFF’s experience advising studies on these tactics over the past two years has resulted in an ever-evolving document tracking all of the best practices that have been successful. This document is currently offered as a resource to potential grantees to begin their recruitment planning, and is posted on the foundation’s website for anyone in the field to consult during their recruitment planning activities. Additional handouts on specific procedures and research needs have also been developed and posted for the field to use (at www.michaeljfox.org/focusonclinicaltrialrecruitment).

The activities the foundation has initiated to date are a start to addressing these issues for the field. With the launch of one project that addresses one piece of the challenge of recruitment, other new objectives that need to be addressed are emerging. The foundation team working in this area continues to amass a list of new initiatives and ideas, and is prioritizing opportunities as human resources allow.

Future anticipated activities include developing a PD coordinator community to share materials, ideas, and lessons learned from recruitment, and assembling an online recruitment toolkit that supports materials creation and messaging for all studies. On Fox Trial Finder, planned developments include making available a study feasibility analysis tool so investigators can search the database as they are designing a protocol to assess the “recruitability” of the study; lightweight versions of study results for the patient community; and improved analytics for trial teams. Physician outreach and education are other major opportunities for increasing volunteer registrations on the site.

Conclusion

We have discussed the strategy development and experience of one disease advocacy organization. We hope that this experience serves as an example for other players involved in drug development to consider opportunities to innovate and create novel partnerships for addressing the roadblock of recruitment for trials systematically.

For site investigators or coordinators, this may mean thinking creatively about recruitment for the next trial and asking the study sponsor for funding to implement novel ideas. For sponsors, it is an opportunity to think broadly and be inventive about how to plan recruitment for the next study. For other disease advocacy organizations, determining if staff can devote some of their time to these activities may be possible.

Considering all of the activities involved in truly functioning as a “department of cures” is a daunting task, and perhaps no one player—MJFF included—may ever fully realize the myriad of functions that serving that role requires. However, acknowledging that we all play a part in moving new therapies through the drug development process, and that this goal is a shared one, can be a pathway to new ways of thinking.

Disruptive innovation, creative partnerships, and a willingness to invest resources to bolster the field have contributed to the early successes in this arena for the foundation’s programs. Over time, the goal is to move the dial on the number of subjects enrolled per month and, eventually, to see recruitment rates increase exponentially.

Imagine a world where having to worry about the expense it takes to recruit is eliminated, because all of the people you need are registered and well classified already. Perhaps it would be possible to cut the recruitment period in half in such a world. What if the rate-limiting step for trial enrollment was a site’s capacity to schedule visits and consent people?

At MJFF, we believe that all of these aspirations are possible if those who are engaged in disease research are empowered to think strategically for the field, take calculated risks to invest, pilot new ideas, and replicate success broadly for clinical trial recruitment. In fact, this is an approach that can be applied to anything else that may stand in the way of getting new therapies to pharmacy shelves for patients and of making much-needed research progress in the field.

References


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