CLINICAL TRIALS RECRUITMENT BEST PRACTICES MANUAL

Introduction

This manual has been developed by The Michael J. Fox Foundation (MJFF) Clinical Trial Strategies team. It's contents were culled from site calls that have informed recruitment planning for several trials that MJFF funds, including the Parkinson's Progression Markers Initiative study that MJFF sponsored and has led the recruitment strategy for. The goal of this manual is to provide trial investigators with a comprehensive look at lessons learned and best practices that have resulted in successful recruitment for PD trials across many site. The majority of the ideas included are from sites in the US. Some of them may be useful for non-US sites "off the shelf," others may need to be tweaked, while others just may not apply. MJFF is consistently working to further develop this document and invites all members of study teams to provide feedback on their experiences to enhance this manual as a resource. MJFF is particularly interested in expanding the manual to include tactics for non-US sites and would especially appreciate insight from investigators abroad about the applicability of some of these ideas. MJFF envisions this as an ever evolving document. Please contact Claire Meunier (cmeunier@michaeljfox.org) if you have ideas or anecdotes that should be included.

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Basic Considerations for all Trials

Unique strengths/challenges of trials and sites

One thing we are certain is true is that one trial is…one trial. And each trial site is unique. Depending on who is being recruited, each trial faces unique challenges and opportunities in attracting subjects to participate. Similarly, individual sites for the same study are very different—some are large academic medical institutions, others are independent PD specialty centers, while others are research focused institutes that specialize in neurological disorders. From the nature of a site's particular structure alone, it is clear that strategies that work at one site to recruit the very same patient population may or may not be successful at another site. Additionally, regional differences, relationships between members of the site teams, the competitiveness of referring physicians in the surrounding area and many other factors influence which tactics will be most successful at a site. Given this, sites are encouraged to select the ideas presented below that work best given their unique situation.

Multi-pronged approach

Across all of the sites and studies we have encountered, the most successful sites share one thing in common: an approach to recruitment that is working on several fronts. The best sites seek to reach the same target demographic in multiple ways. They are also approaching multiple venues to recruit. Marketing 101 has a lesson to share here: someone must "see" a message three times before they internalize it. And it can take receiving the message up to nine times before someone acts on it. Given this, the multi-pronged strategy is crucial to successful and timely recruitment.

Think regionally

All of the ideas outlined here can be expanded to include a broader region. Subjects have reported a willingness to travel up to 5 hours to participate in studies. Outreach beyond your metropolitan area can be a great way to bolster recruitment.

Revisit these ideas regularly

If you are just starting your trial, you may already have great ideas for how you will recruit and be very busy getting those strategies going. In 3-6 months though, you may experience a lull. The ideas outlined here serve all stages of the trial recruitment. If you have a steady stream of interested subjects now, then revisit these ideas later when you are looking to revive your tactics.

Preparing for Study Launch: Branding, Messaging and Materials

Developing a study brand and key talking points to describe the study and who you are trying to recruit is an early investment that is a huge time saver once your trial is recruiting. This is especially true for multi-site studies where every site would otherwise spend a little time thinking about this, resulting in varied messages and inconsistency amongst materials. A centralized approach to developing a core suite of materials before sites are activated to recruit can bolster recruitment at all sites. These materials make recruitment much easier and decrease the challenges of getting others to help you spread the word about your trial.

Developing a study brand

It doesn't have to be anything fancy, but every trial should have a brand that is consistent for all materials. Pick a color and a typeface that your will use across the entire suite of materials.

Developing key messages

Spend some time thinking about the 40,000 foot view and how you want to communicate that to a potential subject, a peer medical practitioner, and the media.

- ***Answer these questions:***
    - Why does this matter? If we get the result we are hoping for, how will the PD field be changed? And how might that help PD patients?
    - What are the selling points of this trial? Why should someone want to participate?
    - What are the challenges in getting subjects to participate in this study? What can we say up front to mitigate any anxiety or concern about participating without raising unnecessary concern?

Creating a suite of materials

Consider creating some combination of the following list of suggested materials. For multi-site studies, it is worth having a coordinated group take the lead on developing well thought out materials that can then be shared across sites.

- ***Patient recruitment material***: brochure, postcard, flyer, etc.
- ***Study talking points.*** These may be useful in media pitches, clinician presentations to patient groups or colleagues, and to guide support group leaders in announcing your trial to their networks, etc.
- ***Materials for referring MD's***: Pocket card, referral form, MD letter, etc.
- ***Press release and study fact sheet***. For studies that have media appeal, develop a boilerplate press release announcing your study launch.
- ***Short and long articles*** about the study to include in your own publications, in association newsletters, etc.
- ***PowerPoint slides to present the study to patient and physician audiences.*** Valuable for consistent messaging at support groups, association meetings, etc.

As you work to create these materials, consider these guidelines: First include a "hook" for why someone should identify themselves and pick this up. Also, don't provide too much information—err on the side of less detail so that you only provide high-level basics that one would need to pre-screen. This is especially true for practitioner materials. Providing too much scientific rationale or detail about the inclusion/exclusion criteria could mean that a practitioner won't read far enough to see your request for subject referrals or, even if they do get to the description of what patients you are looking for but the description is too detailed, the referring practitioner then ends up screening patients out who are viable candidates before they even get referred to you. For subject recruitment materials, also be sure to provide a description of any highly technical or scientific language to demystify it. We are used to talking about repetitive transcranial magnetic brain stimulation, but to a patient that sounds like a very daunting procedure. Finally, patients recognize and want to be affiliated with your organizations. Work with your Marketing/PR office to get official high-resolution logos and the official colors of your organization to use in these on materials.

Establish a 1-800 number and/or website

Identify a central information hub where people can go to learn more about your trial. Make sure that there is a tracking mechanism for inquiries when someone calls. This is the best way to track inquiries to evaluate effectiveness of strategies. Your web strategy may be to direct people to a 1800 number, but all medium to large trials should have a web presence of some sort.

Talking to Potential Subjects

Presenting the Importance of Clinical Research

Add a statement of your belief about the importance of clinical research ultimately benefiting all patients with PD even if the specific outcome of this trial will not serve the patient you are asking to participate. Never say that a trial needs a patient, rather a patient should feel that they have a unique combination of features that potentially qualifies them for an opportunity to participate if they are lucky enough to get in. Presenting a clinical study in such a manner manages expectations. If a study involves procedures that may cause patients concern (such as lumbar punctures (LPs) or imaging), have an investigator or an experienced practitioner confidently demystify these procedures.

- ***Make the case for why the trial matters***. People want a sense of the big picture and the part they can play in it
- ***Believe in it!*** Even (and especially) if your study does not have the immediate appeal of a novel agent or approach, be sure that you convey your belief in its potential.
- ***Be aware of how you communicate with patients*.** Transmit energy and excitement about the nature of the trial.

Tips for Investigators

Investigators are not only a key part of the research team for completing study activities—they are also crucial players in recruitment for studies. Consistently, the sites that are most successful in recruitment for trials have investigators who are active participants in specific activities related to recruitment. Investigators should be "front and center" as much as possible when promising trial leads come into the clinic. At the end of the day, patients value time with a doctor. When asked why they would consider participating in a trial, over half of patients said they would do so to get increased attention and care from a physician or they would participate because their doctor told them to. A major selling point for participating is investigator attention -- this must be showcased up front. Investigators also have an important role to play in physician outreach. Community physicians who are being asked to refer patients to a study want to be contacted by a colleague, not by any other member of the site study team. Investigators should also be key players in developing and executing on a recruitment strategy for each trial. While other members of the study site team may be implementing specific tactics that are part of this plan, the investigator should be an integral part of developing a recruitment plan, brainstorming new ideas to keep the pipeline of qualified leads full and troubleshooting when there is a lull in potential subjects.

- **Key talking points for patients.** As the clinician, it is important for potential subject to be invited to participate in the study by you. As you are reviewing a trial with the patient, explain the pros and cons of participating. Highlight the study as an opportunity and explain its scientific rationale in a way that patients can gain a basic understanding of the possible impact their participation could have. Patients want to learn a about the science of the trial, but be sure to communicate study info they can relate to in lay friendly language.

Tips for coordinators

Coordinators are on the front-lines of communication and connections between subjects and trials. They are the key connectors that make trials happen. Interactions between coordinators and patients are the "customer service experiences" that retains subjects for the life of the study.

- **Encourage discussion about trials in person**. Make every attempt to bring potential subjects into your practice if they inquire about participating in a study. In person conversations are much more personal and provide opportunities for you to respond to any immediate concerns.

In some instances, mailing information about a study without meeting first in person is necessary. Always follow up on your mailing with a call and if an investigator could better address any concerns, have the PI also follow up with a phone call. Even when patients meet with you in person, but want to continue to think about whether to participate, set a timeline for when you can expect to hear from them and follow-up if you don't.

- **Be timely**. Call people back in a reasonable timeframe. If you are inundated with inquiries, set expectations about response time up front by changing your voicemail to say that it could take up to 10 business days for you to respond to their inquiry.

Finding Potential Subjects within Your Institution

In the Clinic

The patients who are in your clinic are the lowest hanging fruit for recruitment. They are loyal to you and your practice. Because these are the easiest leads to convert, it is crucial that sites are thorough in these efforts.

- ***Tag charts of appropriate patients as your site is preparing to be activated.*** If you are seeking controls, consider PD patients who may not qualify, but who have caregivers or loved ones who might be willing to participate on their behalf as controls.
- ***In recruiting de novo patients, reserve priority clinic appointments for newly diagnosed patients so that they get seen in a timely manner.*** Especially in clinics where the wait time for an appointment can be up to 6 weeks, be sure that you don't miss the window of when a patient is unmedicated simply because there wasn't an appointment available.
- ***Inform (and remind) your clinic colleagues of who you aim to recruit.*** Keep your study top of mind by incorporating it into grand rounds and monthly meetings. Also, consider having a research binder in each patient room that is updated regularly to include brief paragraphs about all recruiting studies at your site. While your own trials are often top of mind, sometimes your colleagues' trials aren't. And in academic centers, there may be residents, interns, or medical students who are new to your institution or service and are unfamiliar with your study. One tip for organizing the list of trials in the binder is to list them by disease stage of subjects being recruited (so trials seeking newly diagnosed subjects are listed first).
- ***Develop systems and processes that make referring a patient easy.*** Sites are encouraged to think creatively about developing ways to help colleagues quickly and easily refer patients being seen at your site to clinical studies. One site shared with us that they compiled a list of all ongoing clinical studies in binders and placed a binder in each clinic room, so colleagues could quickly access basic information about recruiting trials when discussing opportunities with patients. The same site also created an email address specifically for referrals; once a physician identified a patient that might be a likely match for a trial, the physician could easily send an email to that address with the Electronic Medical Record number of the patient. A coordinator was responsible for frequently checking the email inbox and 'triaging' emails to prioritize follow up with specific patients. Ensuring that it's easy for physicians to quickly access information on trials and that the process to refer patients is quick will significantly help generate patient referrals.
- ***Equip patients with info about trials.*** This sounds like a no-brainer, we know, but it bears inclusion here. Provide recruitment materials in your waiting room. Replenish them often. Consider including a research binder similar to the one you keep in patient rooms in the waiting

room of your clinic so that people waiting for an appointment can browse the research opportunities at your site.

Leveraging champions of PD/Research

- ***Suggest that enrolled subjects find a "research buddy."*** Newly diagnosed PD subjects can find an age and gender matched control to participate in the study in their honor. When asking patients about this, suggest that they use the rule of 5's: identify 5 people (gets them thinking of more than just one person) who they have known for 5 years (makes it more likely that this person will join them) who are within 5 years of their age (helps with age match) and of the same gender (helps with gender match). Even for PD patients who aren't eligible to participate, but who still want to engage and help, have them approach their loved ones and networks to motivate them to volunteer in their honor.
- ***Consider contacting subjects who have participated in other studies at your site*** (check on your institution's regulations first).

Throughout your organization

One of the biggest opportunities for sites is to leverage the size and reach of the broader organization within which they reside. Reach out to other departments and support functions to support your study. Aside from your clinic, patients who already see a doctor at your center are the next most likely to be inclined to participate in your study, which makes cultivating strategies like the ones below medium-to-low hanging fruit.

- ***Consider tagging charts in other specialties (neuro and outside of neuro) whose patients may qualify as controls***. Also, consider other specialties or services that exist at your site where patients may already be having some of the tests and assessments (i.e. headache clinic patients who are required to get an LP might be inclined to enroll as a control in a study that requires this procedure).
- ***Conduct an Electronic Medical Record (EMR) search to identify qualified leads.*** Most organizations have an EMR that investigators can use to search their entire network for patients with specific diagnostic codes and medication regimens. Utilize this resource for your research. Check in with your IRB about regulations around this, especially as it pertains to actually contacting those leads. If an IRB isn't willing to grant you permission to reach out to potential subjects directly, contact their primary physician in your network and ask them to approach the patient about the study.
- ***Post study information around your site.*** Use this as a checklist for all of the places you need to make sure there is information about your study for each trial you start.
    - Website (for larger medical center and for your site)
    - Advertisements and flyers throughout your site (bathrooms are a good place to capitalize on a captive audience)
    - In your waiting room (remember to replenish supplies)
    - Create an "information wall": a bulletin board with information on research/clinical trial opportunities, support groups, PD classes, and other postings useful to your patients
- ***Connect with clinical and research colleagues.*** Host a noon conference or grand rounds. Be sure that satellite locations affiliated with your site have key information about the study. Utilize institution practitioner email lists to notify your peers that you are seeking a particular group of patients. At one site that was recruiting controls for a study, they sent an email asking physicians

to refer *de novo* subjects. In response, they got emails from 5 physicians who themselves have volunteered to be screened as controls.

- ***Participate in community events*** (i.e. health fairs, patient days, etc). Leverage opportunities to build awareness about PD to talk about research opportunities at these events.
- ***Organization-wide publications.*** Publications like the medical center's annual report, weekly e-newsletter and monthly update to staff incorporate spotlights on the projects going on within your organization and patient stories. Contact the appropriate group to get your trial to be the story.
- ***Media.*** Media enables a site to cast the next wide and generate a lot of calls about a study. Unfortunately, the yield on these inquiries is often quite low. Media is also hard to get. In our experience, the best use of media is to generate interest from controls. We do not recommend a media campaign to attract PD patients to a study—the message about your trial is too specific for such a broad audience and could create a major burden in responding to inquiries that don't end up being good leads.

  If you are planning a media campaign, consider the questions below to get started. Work with your media office to see what might be possible. And if you can't get coverage in the media, don't sweat it. Not all trials make media-friendly stories and there are a wealth of other strategies that can be pursued instead.
  - ***Is the study media-appropriate?*** Think about the "human interest" component of your study. Would the general public be interested in reading about this research? Is it "lay-friendly"? Would you be able to tell a good story with the rationale for this research? If the answer is yes, work with your media office to explore this further.
  - ***Share the suite of materials you have developed and other assets.*** The number one thing that you can do to increase the likelihood of getting coverage for your trial is to provide you media office with the materials they need to pitch a story. To start, a press release and fact sheet about your study are core items. If you have these, approach your media department to try to get them interested. Another helpful resource in approaching your media office is to have a study subject in mind who the media office could include in an interview if a media pitch is successful. If the media office takes this route, they will work with you and the subject to get a consent form signed. We recommend that you wait until you know if media will take place before asking a subject about participating in media, as you will want to avoid over promising in this arena.
  - ***Where to target for your pitches.*** Media offices also appreciate some forethought about where a story might be appropriate. You should have a few outlets in mind when you approach your media office about this. They will have great ideas too, but you should go in with some preliminary ideas. And remember, sometimes getting a good article in smaller publications can be as or more fruitful than a small blurb buried in a large paper.
  - ***If all else fails…*** If a media pitch about your trial isn't getting picked up, consider doing a more general article about Parkinson's disease, including the signs and symptoms of the disease. Raising awareness about early signs, your specialty in this area and center may still generate good leads.

Investing for the long term

The following ideas are admittedly a bit more resource intensive. Some are costly, some require substantive time to implement. That said, they are proven to be effective strategies for trial recruitment in the long term. In the short term, they raise the profile of your center within your community, connect

you to patients who you can keep reminding about your work and are excellent opportunities to continually prepare people to be asked to participate in research when a trial they qualify for comes along. We hear all of the time that sites want to do many of these things but that recruitment won't improve in the shorter term. Investments like these may be harder to get off the ground and take time to prove themselves, but once they are working they can be an endless source of new trial traffic.

- **Discuss the mission of your center at every visit**. Remind patients every time they come in that the goal of your clinic is top notch clinical care and research science. Integrate "the latest research findings" into your treatment recommendations for patients to make research something that is important to their disease experience. By including this in every visit, people are primed to be approached about participation in research when they are a good fit for a trial.
- ***Create a database of patients who express interest in research participation.*** Include clinical features so that you can identify suitable participants for any particular protocol. Include individuals identified at support group meetings and public presentations as well as in your practice. (Check on your institution's regulations first.)
- ***Initiate an annual patient/caregiver symposium for people with PD.*** Resource intensive, we know, but what better way to showcase your center? This is a prime opportunity to feature best approaches to care, promote the unique offerings of your center and, of course, to discuss research opportunities.
- ***Create a PD 101 group at your center*.** One site we talked to has a multi-session class they offer once a quarter to bring newly diagnosed patients and caregivers together with their peers to understand the science of PD, discuss treatment options, share day-to-day experiences, and explore research opportunities. For sites that do a lot of *de novo* studies, this is a great feeder.
- ***Profile the study at the end of exercise and other classes your site offers.***
- ***Send a center newsletter.*** Collect mailing and/or email addresses and send quarterly newsletters to your constituents. Highlight the story of a subject enrolled in research, talk about the outcomes of a study that is just wrapping up, introduce researchers in your practice and showcase their work, and, of course, mention the studies at your site that are recruiting. This keeps your practice on their radar. Consider a similar mailing for MD's—this is a great way to begin to build a referral network (more on that below).
- ***Develop a practitioner recruitment network*.** Every site we talk to wants one of these. And a few sites have successfully developed one. Having physicians and other health care providers in the community who refer to trials is perhaps the best way outside of your clinic to get qualified leads for your trials. But we realize this isn't easy—mostly because of competition and the fear of patient's clinical care being "poached" by the research site. While this cannot be overcome in its entirety, here are a few tips for trying to get this strategy off the ground. And remember, if you can just get 2-4 physicians who will refer to you regularly, that could be a lot of referrals over the years.
    - ***Who to reach out to.*** To start, determine who in your community sees the most PD patients. Expand your definition of referring physicians to referring practitioners. Reach out to NP's, PA's, Allied health practitioners, VA's, etc. Naturopathic physicians are also a great resource for newly diagnosed PD patients and controls who are research-inclined and not on meds. With all of these groups, there doesn't tend to be as much of a direct threat for poaching as with other care providers. Also, consider physician outreach to practitioners at hospitals that treat the uninsured—they often welcome the additional attention to a specialist that can be provided through trial participation. Finally, expand to neurologists and select primary care practitioners as appropriate.
    - ***What to say***

- In areas where your colleagues will be receptive to referring to you, highlight that you are the PI (someone they know and respect) and ask directly for their support in this way.
- In areas that are highly competitive, consider removing your site name and contact info entirely and simply directing people to a study 1-800 number or website.
- Make it as easy as possible for the physician to refer. You have to do much of the work for them by providing easy access to the basic criteria for inclusion in the study and by making the act of referring simple. Distribute a pocket card and fax referral form when speaking to potential referral practitioners.
- Assure the colleagues you are reaching out to that your goal is solely to enroll the patient in research. Consider using language like this: "Please be assured that any person you refer will remain a patient in your practice and you will continue to provide their clinical care. We will provide only the care necessary to conduct the trial in accordance with the study protocol and to ensure subject safety. We will refer the patient back to you as their primary care provider for any clinical issues."
- Also, state your plans to provide test results and findings about the patient back to the referring practitioner. For community physicians, knowing that someone if going to spend time conducting extensive tests and assessments on their patients and provide that information back to them is often a major selling point for referring a patient. Follow this up by actually doing this after each study visit.
- Expand the scope of information you provide when reaching out to your colleagues by including more than info about your study. Provide information about PD 101 classes, patient symposia and/or support group information. Even if someone in your audience doesn't directly refer patients to your study, they may give their patients the info for your classes/groups (where you can then tell them about your study).

- ***How to reach out.***
  - Present info about the study at local/regional/national neurology meetings, CME courses, etc. Bring patient recruitment materials to the meetings for practitioners to take back to their practices. Create a list of all trials going on at your center and bring a ready supply to presentations for attendees to take back to their waiting room.
  - Send out MD-to-MD letters
    - When sending via email, have it come from the PI (not his/her admin)
    - You may be able to get the names and addresses of neurologists in your recruitment area by contacting your state neurological association. Some state associations provide mailing labels as part of membership.
  - Hold an event to educate physicians about your work and make a case for why they should refer
    - Send a packet of materials to those who aren't able to attend so that they still have the information.
- ***Follow up!*** Once you get a physician who refers to you, the ball is in your court to get them to refer again. Send a thank you note to the referring practitioner. Offer them something valuable in return: Share test results, hold quarterly conference calls updating them on the trial and your center's activities, invite them to MD events, offer to acknowledge them in the study first publication, etc. This is also a perfect opportunity

to reiterate that your intent is only to assume a patient's care as it pertains to this research study and that you will send the patient back to them for all clinical care. If you say this to them, be sure that you actually do the follow up.

Recruitment in your community

Reaching out to groups that support the care of PD patients in your community is another great way to recruit for studies. Since the people who lead and organize support groups are new contacts or ones who you may not interact with regularly, this outreach may require some extra work.

Support group connections

Support groups are always looking for speakers, newsletter content, information/handouts, etc. Fill those needs for them by offering to speak at their next meeting, provide an article about your study, provide recruitment materials. Cast the net wide for your support group outreach. Depending on your location, patients may be willing to travel up to 5 hours to get to your study site. For support groups that you cannot attend in person, send packets of recruitment materials with a cover letter and talking points for the leader to use when they present your study. Create a list of all trials going on at your center and mail each support group leader 20 copies. Even if you are looking for newly diagnosed patients and worry that they won't be in the support group, still reach out—someone who has just been diagnosed is likely to connect with someone who has PD who might be in the room at the support group. Also, support groups are an excellent source of motivated caregivers (=controls!).

Other PD groups

In addition to support groups, there are several national PD organizations and local PD groups that can be approached to help with clinical trial recruitment. Using the newsletter blurb you developed at the start of your study, approach these groups and ask if they will feature your study in their next newsletter. Having pre-written content will increase your likelihood of getting your story included. Consider some of the same tactics outlined in the support groups section for partnering with these groups: provide them with study recruitment materials, offer to speak at their event, etc.

Pharmacies

If your trial is recruiting someone on a specific medication, ask your local pharmacist to share a flyer about your study each time s/he dispenses that specific medicine.

Once Subjects are Enrolled (and things to talk about when they are thinking about enrolling)

Be flexible

Consider holding evening and weekend visits to accommodate study participants who are employed or have busy schedules. Stay late one day a week to hold after hours recruitment calls if needed.

Be timely

Provide timely reimbursements for accommodation, travel, food, stipends, etc. When you promise payment up front, subjects expect to be paid back within a few weeks at the most.

Make it worth the time commitment

Patients like to feel appreciated for their time. Consider offering "touch points" throughout their involvement in the study that will make enrolling in the trial a beneficial experience. These may include:

Give-away or take-home items, Birthday/Study anniversary cards, exclusive events for study participants.

Adhere to the Patient Bill of Rights

Differentiate your center by touting your compliance with the PD Pipeline Project's Patient Bill of Rights. Tell patients about your adherence to this in conversations and provide them with a copy of the document in any study materials. http://www.pdpipeline.org/advocacy/rights.htm