Accelerating Clinical Trials

Best Practices for Recruitment and Retention

"When the cure for Parkinson's is found — and it will be — it will be because of all of us."

–Michael J. Fox

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It takes hundreds, and often thousands of people to design a clinical trial and carry it through to completion. On the medical team, this includes researchers, clinicians, nurses, technicians, study coordinators, office staff and many more. In the broader community, clinical trial teams reach out not only to people with Parkinson's, but also to care partners and families, support groups, primary care physicians and other local health care providers. At the center of it all are the study participants.

This manual takes the participant journey as an organizing principle for optimizing clinical trial design. From recruitment through post-trial follow-up, participants volunteer to travel on a highway leading to better lives for people with Parkinson's disease. Along the way, they interact with both health care personnel and people in their community to help them stay the course. On-ramp encounters lead to engagement and enrollment. But participants may encounter off-ramps — situations that lead to dropping out — as well.

By understanding participants' needs and the obstacles they face in their journey, and by taking into account the insights of a wide range of stakeholders, clinical trial designers can streamline participant enrollment and ensure that volunteers continue through to the trial's end. Here, we provide a step-by-step, patient-centered approach to recruiting and retaining trial participants. Our guide takes advantage of new technologies that have increased patient awareness and enthusiasm for clinical trial participation, made data collection easier and opened new routes to novel discoveries.

In addition, we have assembled a toolkit that anyone designing a clinical trial can customize and use to present to the Parkinson's community. The task of recruiting and retaining study participants need not be overwhelming. These practical resources can help support progress in Parkinson's research.

Chapter 1

Clinical Research Design and the Participant Journey

Objectives

+ Describe the participant journey and how it informs clinical trial design

+ Characterize key stakeholders and how they can provide insights into the participant journey

+ Outline steps in the formation of a key stakeholder working group and critical junctures for input

+ Share a case study that illustrates how a key stakeholder group can be used to improve clinical trial design

In recent years, innovations in clinical trial design, combined with new technologies, have made it easier for patients to find out about and participate in research. At the same time, a trend toward including more stakeholders in trial design has led to novel recruitment methods. More and more, clinical trial design puts patients at the center, focusing on their needs — increasing understanding of how to engage research participants and also what discourages participants from joining or completing a trial.[1, 2] This chapter explains the importance of key stakeholders for understanding the participant journey, and outlines ways to obtain stakeholder input for a patient-centered clinical trial design process.

[1] https://www.biopharmadive.com/news/5-trends-changing-clinical-trials/437416/
[2] http://www.appliedclinicaltrialsonline.com/perspectives-past-present-and-future-clinical-trials

Audience Key

The icons below appear throughout the manual and are intended to highlight specific sections that are most useful for readers as it relates to their role in the clinical trial process.

(SP) Sponsor

(CR) Contract Research Organization (CRO)

(MC) Multi-center study

(SC) Single-center study

Describing the Participant Journey

(SP)

In broad terms, the participant journey refers to the process by which an individual navigates a health care system or systems. Mapping this journey is a helpful way to gain insights into the areas where services are provided successfully and where this could be improved. The ethos of clinical trial design is increasingly embedded in patient centricity, and journey mapping has become an important tool that designers of clinical trials can draw upon to better understand how they are meeting the needs of their participants, and where there are gaps. Ultimately, this tool helps improve the design, planning and implementation of research studies. Key components of a participant journey in the context of clinical research participation include:

+ **Goals:** an individual's motivations or the health outcomes they hope to achieve. For example:

  – Motivations: altruism, speed a cure for Parkinson's disease, advance research, help a loved one

  – Health outcomes: desire for a better delivery mechanism for medication, wanting to improve the quality of the daily lived experience, or wanting to experience fewer motor or non-motor symptoms

+ **Off-ramps:** challenges that may prevent individuals from achieving their goals and prompt them to exit the roadmap of clinical research participation. For example:

  – Not hearing back from clinical trial teams; not being able to attend appointments on weekends or after work hours; not being provided educational materials in comprehensible/lay terms; not having transportation to and from appointments; not having materials translated into an individual's native language; not being able to take regular medications while participating in a trial or study

+ **Touchpoints:** encounters that an individual may have with an organization throughout the participant journey, including both advertisements and human interactions. For example:

  – Viewing a clinical trial posting on Fox Trial Finder (foxtrialfinder.org); calling a toll-free telephone number and speaking with a clinical trial coordinator; checking in with a receptionist at the clinic; meeting the study principal investigator or coordinator for the first time

Identifying and Engaging Key Stakeholders

(SP) (CR)

Key stakeholders are individuals and organizations that have an interest in or are affected by your clinical trial and its results.[3] It is important to bring key stakeholders into the clinical trial design process as early as possible, as they can provide insights on participant or site goals, and potential off-ramps and touchpoints throughout the clinical trial process. In addition to study sponsors, key stakeholders that should be involved in the design process include:

+ **Trial team representatives:** individuals who represent the clinical trial sites implementing your study. To identify these representatives, start by making a list of the characteristics or infrastructure required for successful study implementation (e.g., access to the target population, support group connections, partnership with a clinic). Then reach out to institutions that have those characteristics and gauge their interest in consulting on your protocol as part of a key stakeholder working group. One or two individuals from each institution should be invited to participate as part of a study working group and may include:

  – Principal Investigator
  – Study Coordinator

[3] https://www.cdc.gov/std/Program/pupestd/Identifyingpercent20andpercent20Determiningpercent20Stakeholders.pdf

– Research Assistant

– Registered Nurse/Coordinator

+ **Patient representatives:** individuals or advocacy groups that represent patients participating in the study. To identify these representatives, start by making a list of patient or advocacy organizations that have access to your target population, and will have insights into this population's attitudes and motivations toward participating in research. Once you have identified these groups, gauge their interest in consulting on your protocol as part of a key stakeholder working group. One or two individuals should be invited to participate and may include:

– Engaged patient, such as a Fox Trial Finder ambassador or a Parkinson's Advocate in Research activist

– Community liaison, such as a social worker, or health educator

– Communications specialist, such as a public relations coordinator or manager, or a social media analyst

When engaging key stakeholder groups make sure to: 1) qualify the type of input and perspective you are seeking; 2) discuss the potential role and/or individuals who are best-suited to contribute; and 3) explain the requested level and length of commitment for participation.

Gathering Input on Key Protocol Components

(SP) (CR)

Key stakeholder input can be invaluable in these areas:

+ **Recruitment and Enrollment**

– Can eligibility criteria be expanded to include more participants? If so, can this be accomplished without jeopardizing study design or key regulations?

– Do sites have access to the target participant population? If so, what are the planned outreach methods?

– Will a randomized control design affect the ability to recruit? What is the treatment that the control arm will receive, and will this be acceptable to participants?

– What, if any, side effects might participants experience from the study drug? Will this deter participation?

+ **Study Procedures**

– What does the site workload entail? Could the order of assessments or schedule of activities be streamlined without decreasing scientific rigor or causing harm?

– Is it feasible to implement a blinded or double-blinded study? Would this increase burden or workload on sites?

– Would additional study personnel be required to facilitate implementation of the schedule of activities requested?

– What is the study burden on participants? Could this be reduced? If so, how might this be accomplished while adhering to the study design?

– How frequent are participants' study visits? Can any be conducted at home or online?

– Are the procedures physically or emotionally taxing for volunteers or their care partners? Are there supports (e.g., financial, educational or physical) that can be provided to facilitate participation?

+ **Trial Sites**

– What are the most and least important qualifications for clinical trial sites?

– How are qualifications weighted and evaluated during site selection?

– Are there particular sites, institutions or geographic regions whose participation would add scientific, strategic or operational value?

– Are there any plans to contract or subcontract with additional sites if primary site(s) is/are unable to recruit target participant population?

Engaging Key Stakeholders by Forming a Study Working Group

The Clinician Input Study (CIS-PD) is a trial sponsored by The Michael J. Fox Foundation (MJFF) that seeks to assess the impact of wearable and mobile app data on clinical decision making for individuals with Parkinson's disease (PD). Participants logged information on symptoms and medications via smartphone application; smartwatches collected movement data. Over the course of the study, an online dashboard allowed participants' treating clinicians to assess the utility of the patient-reported and movement data on clinical care management. Computational scientists used the data to identify movement signatures of PD, (i.e., movements specific to PD) that are recognizable when an individual is wearing a smartwatch.

Several factors contributed to the decision to form a study working group, including the novelty of data collection methods, the in-home study design and the impact on a variety of stakeholders. The group's goals were to identify and address potential study off-ramps as well as study design successes. To accomplish this, the working group included individuals participating in, implementing, or affected by the outcomes of the CIS-PD study. The table below lists the key stakeholder representatives, their perspectives and the areas of study design that their perspectives informed:

Representative(s)	Perspective	Key Areas for Consideration
+ Patient Representatives + Community Engagement Representatives – MJFF	+ Those who would be participating in the study	+ Participant study burden + Study logistics
+ Principal Investigator + Project Managers – MJFF + The Technology Platform Provider + Computational Scientists + The Data Management Unit + Clinical Coordinators	+ Those who would be implementing the study	+ Trial team burden + Technology capabilities and Imitations + Data collection methods + Clinical endpoints
+ Patient Representatives + Computational Scientists + Clinical Coordinators	+ Those who would be affected by study outcomes	+ Value to and utility for clinical care management

The working group reviewed all study documents including the research protocol, informed consent documents, case report forms and procedure manuals. This review process revealed that a series of the assessments proposed by the computational scientists was both lengthy and potentially burdensome for patients and coordinators. Based on the working group feedback, the protocol was refined to ensure that there was balance between data collection and feasibility.

Key Considerations: Incorporating Digital Health Technologies into Your Clinical Trial

Digital health technologies have the potential to modernize the way clinical trials are conducted, and to make them more informative and efficient for sponsors and less burdensome for patients. From including telemedicine visits into study protocols to monitoring patients remotely through wearable devices, digital health technologies are rapidly changing clinical trial best practices.

A wide variety of digital health technologies, including mobile phones, wearable devices, tablets, personal digital assistants, sensors and computers, can be used to support novel data collection in clinical research. While planning your trial, be sure to consider how these tools may improve your study design:

+ **Send e-reminders through text message or email:** Automated reminders for participants to complete certain protocol requirements, such as taking medications or scheduling an appointment, can improve compliance of participants while introducing little burden to sites.

+ **Collect patient-reported data through an app or online:** Using technology to administer electronic patient reported outcomes* (clinically validated scales that have been optimized for administration on a smartphone, tablet or computer) can gather information remotely and provide insights into participants' experiences outside of the clinic.

+ **Collect novel datasets via wearable sensors:** Wearable sensors have the potential to provide objective data about participants' experiences in and out of the clinic. This collection method can gather massive amounts of data at fine granularity and requires minimal patient engagement.

+ **Conduct telemedicine visits:** Instead of having participants travel to the clinic for a study visit, consider if evaluations can be done through telemedicine to reduce patient and site burden.

Chapter 1
Key Takeaways

+ Use the participant journey to map out successes, potential challenges and areas for improvement in your clinical trial design.

+ Involve key stakeholders early in the clinical trial design process to enhance feasibility and acceptability by sites and participants.

+ Consider ways in which technology could be incorporated into your trial to enhance the participant experience.

Underlined words indicate a commonly used term. Find the definitions in the glossary, starting on page 42.

Chapter 2

Assessing Opportunities and Challenges

Objectives

+ Highlight the role of clinical trial sites for increasing study feasibility and patient acceptability

+ Explain how to define and prioritize site characteristics to enhance study implementation

+ Provide methods to evaluate sites based on those criteria

+ Share examples of Parkinson's disease trials that evaluated potential study sites for opportunities and challenges and incorporated this information into the site selection process

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The clinical trial site is the source of crucial touchpoints in the participant journey with clinical research. To be truly patient-centric is to support sites so they can provide participants with a successful and rewarding research experience. This can be accomplished by involving sites early in the study design process (e.g., as stakeholders in a study working group), obtaining their insights on potential challenges and opportunities that may affect study feasibility.

Another way to provide support is by identifying and defining site-level characteristics or qualities that will enhance the likelihood of successful study execution. Having these discussions early will help sites and study sponsors alike to understand expectations, and will ensure greater alignment throughout the trial. In this chapter, we explain how to work with sites to identify potential opportunities and challenges in the study, how to use these insights when selecting sites, and how Parkinson's studies undertook this approach to ensure successful implementation of a complex protocol.

Evaluating Opportunities and Challenges in Study Design
(SP) (CR)

In clinical research, study sites are unique places where the science and the participants come together. By looking closely at what happens at this meeting place, site personnel can identify potential challenges or opportunities for a study's feasibility, and for its acceptability to patients.

+ **Challenges:** potential barriers in the protocol (such as overly stringent eligibility criteria, lack of accessibility to technical instruments)

or off-ramps (high frequency of visits, invasive procedures) that could make implementation difficult, or discourage participants from volunteering and/or completing the trial

+ **Opportunities:** incorporating into the protocol ways to make implementation or participation easier (telemedicine visits, incentives, provision of transportation, access to personal health information)

+ **Study feasibility:** an indication, based on the evidence gathered, as to whether or not a study is viable and stated objectives can be achieved[4]

+ **Participant acceptability:** the level of effort (e.g., time, physical and emotional energy) that a participant would need to put forth in order to participate in a study, and the potential benefit perceived from participation (e.g., how much this will advance the field and additional care they may receive)[5]

[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3146075
[5] https://bmchealthservres.biomedcentral.com/track/pdf/10.1186/s12913-017-2031-8?site=bmchealthservres.biomedcentral.com

Breaking Down Transportation Barriers to Research Participation

Background

In January 2017, The Michael J. Fox Foundation launched a survey to assess the need for transportation infrastructure at clinical trial sites. Using Fox Trial Finder, MJFF's online clinical trial matching tool, 843 clinical trial sites in the U.S. were contacted to understand how transportation access impacts participant recruitment, and what kind of transportation participants would find most helpful. Of the 49 sites that responded, 95 percent reported that transportation infrastructure would improve recruitment efforts, and 63 percent felt it would ensure all studies recruited on time. Eighty-four percent of respondents reported that a taxi, livery or ride-sharing service partnership would be the preferred transportation infrastructure.

Data from the survey was used to inform the design of a transportation intervention that is being tested via the Parkinson's Disease Trial Recruitment Innovation (PD-TRI)

project. PD-TRI is an MJFF-funded pilot study aimed at reducing barriers and enhancing facilitators to clinical trial recruitment.

Methods

Sample

To participate in PD-TRI, project sites had to be based in the U.S., be geographically diverse and have large clinical research portfolios. One of the three selected sites, Beth Israel Deaconess Medical Center (BIDMC) in Boston, MA, elected to implement a partnership with the ride-sharing service Lyft Concierge.* The study principal investigators, Samuel Frank, MD and David K. Simon, MD, PhD, felt that providing round-trip transportation to research appointments would alleviate stress and logistical challenges for study participants (e.g., finding parking, relying on a care partner for transportation, traveling long distances).

Table 1. Distance, Cost, and Time Spent on Lyft Concierge Rides (n = 7)

	Minimum	Median	Maximum	Average
Round-trip cost	$28.54	$72.15	$234.08	**$126.52**
Distance traveled (miles)	6	40	157	**67**
Coordinator time spent arranging rides (minutes)	2	5	15	**7**

*https://www.lyft.com/business/patients

Graph 1. Participant Satisfaction with Rides (n = 5*)
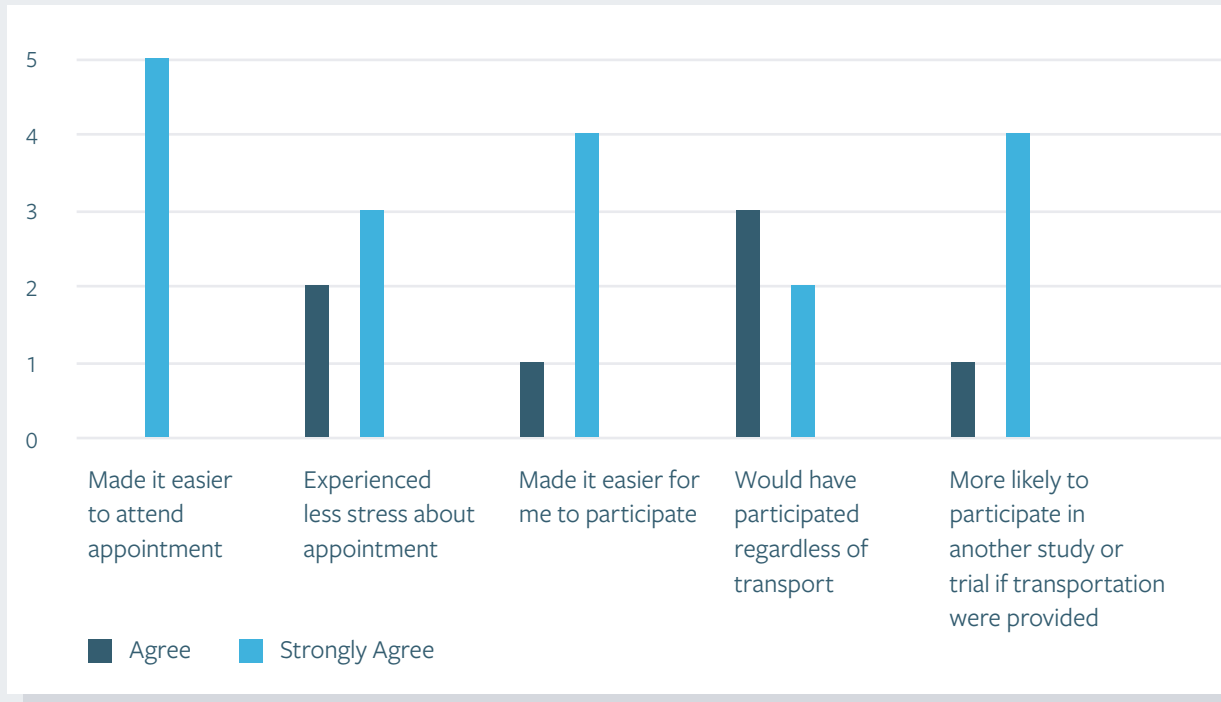
Data are provided only for individuals who received transportation. Options to disagree and strongly disagree were provided, but were not selected by any participants.

Materials

BIDMC used a template to collect data on the cost of the service and the coordinator time required to arrange it, and assess the impact of the transportation service on recruitment. BIDMC also used a study satisfaction survey to gather insights on participants' experience in the study and use of the transportation service. (To view and download an example of a study satisfaction survey, visit michaeljfox.org/ResourcePack.)

Design and Procedures

To partner with Lyft Concierge, BIDMC signed a terms-of-service agreement and implemented a payment system. To use the Lyft Concierge service, coordinators worked with each study participant to determine a pickup location. The coordinator then arranged the ride in advance using a simple web portal. This removed the need for study participants to have a smartphone or online connection. After completing the ride, Lyft Concierge could either charge an institutional credit card or send a monthly invoice to the clinical trial site, thereby removing the stress or logistics of payment from the study participant.

To protect patient privacy, Lyft Concierge allows sites to provide an alias or only the patient's first name when requesting rides. If a site happens to provide a person's full name, the driver receives only the first name and last initial. Moreover, passenger information disappears from the driver's phone once the ride is complete. To ensure the use of Lyft was ethical and compliant with patient privacy regulations, BIDMC developed a protocol explaining Lyft Concierge that was approved by its Institutional Review Board (IRB).

Data Collection

After a preliminary phone screening to determine study eligibility, individuals were offered rides via the Lyft Concierge service. Data on individual acceptance of transportation, cost and timeliness of rides, and coordinator time spent arranging rides were collected via the template. Participants filled out a study satisfaction survey at their baseline visit to assess the impact of transportation on their decision to enroll in the study.

Results

Preliminary data from the BIDMC and Lyft Concierge partnership are provided in the table and graph below. Data from only one BIDMC study are provided, as recruitment for other studies was limited during the PD-TRI study.

Discussion

Initial results provide insights into the impact of providing transportation on clinical trial recruitment efforts:

+ Individuals who live farther from the clinical trial site seem more likely to accept rides, indicating that transportation infrastructure may help clinical trial sites engage with harder to reach populations and broaden their recruitment networks.

+ While providing transportation may seem expensive, the average cost per ride is $63.26. This figure is quite small in comparison to the average total costs of a Phase III clinical trial (between US $11.5 million [dermatology] and US $52.9 million [pain and anesthesia]).[7]

+ Coordinators spend a minimal amount of time and effort to coordinate rides, and from the patient satisfaction surveys, this service appears to provide a great amount of benefit to study participants. Providing this service may help mitigate study attrition.

+ Although study participants indicated that they likely would have participated in the current clinical study even without being offered transportation, they responded very positively to the service, with all participants reporting that the rides made it easier for them to attend appointments. Also, 80 percent of respondents said they would be more likely to participate in another study in the future if transportation were provided. This indicates that providing transportation not only helps recruitment, but also is an asset for long-term community engagement.

+ Third-party ride services can be used in a manner that protects participant confidentiality.

Key Considerations for Sites Contemplating Transportation Partnerships

+ Clinical sites seeking to establish a partnership with a transportation service should request contractual materials from the potential partner, share these with internal grants administrators for review and seek IRB approval.

+ Factor in additional time prior to study start-up for contract negotiations and testing any software or processes associated with the partnership.

+ Develop detailed protocols that determine when and how often individuals will be offered rides, and whether they will be offered transportation for visits throughout the full duration of the study.

+ Create systems to evaluate your transportation service and determine how it impacts recruitment at your site.

[7] http://journals.sagepub.com/doi/abs/10.1177/1740774515625964?journalCode=ctja

Prioritizing Site Characteristics

(SP) (CR)

Evaluation of the study design provides an opportune time to identify and prioritize site level characteristics. Characteristics that mitigate barriers or off-ramps should be considered the highest priority and essential to study success. Characteristics that facilitate implementation or participation should be considered beneficial, but not critical to study success. In general, only two to three characteristics should be prioritized as essential, so as not to define site characteristics too narrowly and risk inadvertently overlooking sites with sufficient capacity.

Site Characteristics Prioritized as Essential or Beneficial

Priority Level	Barrier or Facilitator	Example	Site Characteristic
Essential	Barrier	Difficult-to-reach target population	Site has access to the population of interest
Essential	Barrier	Protocol centers on highly specialized analysis of DaTscans	Extensive site experience implementing DaTscan imaging assessments; or commitment by study team to implement standardized training on use of DaTscans during onboarding process
Essential	Barrier	Highly complex protocol that requires time-intensive procedures	Access to and availability of staff resources
Beneficial	Facilitator	Provision of transportation services to and from appointments	Site has existing relationship with transportation service or has sufficient funding for travel support
Beneficial	Facilitator	Minimal effort required to participate in the study and a high volume of volunteers is expected	Site has a comprehensive recruitment tracking system to identify who has been contacted and who needs follow-up

For additional support on ways to engage with hard-to-reach and underrepresented populations, contact trialsupport@michaeljfox.org

Assessing Sites Based on Priority Characteristics

(SP) (CR)

Developing a questionnaire that outlines the prioritized site-level characteristics (essential and beneficial) will enable you to evaluate sites based on a series of benchmarks. Incorporating specific criteria that speak to the characteristics (e.g., access to sub-populations, experience of site staff and availability of machinery) will make it easier to assess and rank sites. A case study examination of the Systemic Synuclein Sampling Study describes how one team evaluated their study design, identified and prioritized site level characteristics, and then incorporated those characteristics into a site assessment template.

S4 Study Site Selection

Background

The Systemic Synuclein Sampling Study (S4) is a multicenter, cross-sectional, observational study sponsored by The Michael J. Fox Foundation. The primary objective of the study is to better understand the progression of Parkinson's disease (PD) by identifying the optimal biofluids and tissues for measuring the protein alpha-synuclein outside of the brain as a potential biomarker in individuals with PD. The secondary objective of the study is to create standard operating procedures for the collection and assessment of multiple tissues and biofluids to better understand alpha-synuclein's potential as a biomarker for PD. (To learn more about S4, visit michaeljfox.org/s4.)

Study Design

Participants

S4 sought to enroll 80 participants meeting the following characteristics [Table 1]:

Table 1. Target Enrollment, S4 Study

Target Enrollment (n =)	Participant Characteristics
20	Individuals with early PD not requiring dopamine replacement therapy
20	Individuals with moderate PD on dopamine replacement therapy without motor fluctuations
20	Individuals with advanced PD with motor fluctuations
20	Controls

Procedures

The section below provides a condensed overview of the procedures that study participants underwent as part of S4. For additional information on the procedures and scientific rationale used in S4, please refer to the study report.*

+ **Screening Visit**

  – Study staff informed and consented study participants for participation (i.e., study purpose, procedures, potential risks and benefits were explained, and consent to participate was obtained). Their medical and family histories and any medications were reviewed. Participants' vital signs were taken, and a general physical and neurological exam were performed. All participants underwent MDS-UPDRS, Hoehn and Yahr, MoCA, SCOPA-AUT and UPSIT exams. Individuals with PD received Modified Schwab & England Activities of Daily Living Scale and PD stage assignment.

+ **Biofluid Collection and Skin Biopsy Visit**

  – Whole blood, serum and plasma were collected through routine venipuncture.

  – Cerebrospinal fluid was collected through lumbar puncture under local anesthesia.

  – Saliva was collected through 20-minute active drool collection.

  – Approximately four samples of thigh and upper back/shoulder skin were biopsied using skin punch under local anesthesia.

+ **Colon Biopsy Visit**

  – Approximately eight samples of colonic tissue were biopsied from study participants using routine clinical procedures.

+ **Submandibular Gland Biopsy Visit**

  – Approximately five samples of submandibular (type of salivary) gland tissue were biopsied using a 16-gauge needle inserted through the neck under local anesthesia.

Site Selection

The number and type of procedures, as well as the variation in recruitment target population, made the S4 research protocol highly complex. The S4 Steering Committee was aware that this complexity was a potential barrier to successful study implementation and determined that careful selection of clinical sites would help to mitigate this issue. To enhance the site selection process, the S4 Steering Committee: 1) identified and prioritized site level characteristics necessary for study implementation; 2) developed a checklist to evaluate sites in person; and 3) conducted in-person site visits.

+ **Identified and Prioritized Site-Level Characteristics**

   The characteristics identified by the S4 team as most critical to study implementation were:

   – Site personnel experience in implementing clinical studies that involve collecting biospecimens

   – Site-level infrastructure

   – Access to the population(s) of interest

   Each of these characteristics addressed an area of complexity in the research protocol. Experienced site personnel provided additional confidence around the ability to conduct study procedures that were both precise and invasive. Strong site infrastructure ensured that samples were collected in a standardized manner and mitigated concerns around data quality. Access to the population(s) of interest ensured

greater success in recruitment and reduced trial delays. This information was assessed by asking invited clinical sites to complete a site interest form. The forms were then evaluated and prioritized by the S4 Steering Committee.

+ **Developed an Evaluation Checklist**

   The S4 Steering Committee created a checklist that was broken out by the three priority characteristics (experience, site-level infrastructure and access to the population of interest). Within these categories, specific criteria were listed that provided a measure of how well the site ranked on that characteristic (level of experience, type of equipment, access to storage, etc.). (For more information on this checklist, email trialsupport@michaeljfox.org.)

+ **Conducted In-person Site Visits**

   S4 Steering Committee members visited each of the sites under consideration based on their responses to the site interest form and, using the checklist, evaluated them on the priority characteristics. Sites were selected to participate in the S4 study if they adequately met the criteria for participation, including documented experience collecting biospecimens from a PD population, site infrastructure requirements (such as collaborations with gastroenterologists and ear nose and throat specialists) and recruitment plans for the population of interest.

Table 2. Procedure Completion Rates, S4

	Total Enrolled, N	Blood Sample, N (%)	CSF Sample, N (%)	Saliva Sample, N (%)	Skin Sample, N (%)	Colon Sample, N (%)	Gland Sample, N (%)	Evaluable Subjects*
Early PD	20	19(95%)	16 (80%)	18 (90%)	18 (90%)	19 (95%)	18 (90%)	18 (90%)
Moderate PD	20	20 (100%)	18 (90%)	20 (100%)	20 (100%)	20 (100%)	20 (100%)	20 (100%)
Advanced PD	21	21 (100%)	20 (95%)	19 (90%)	21 (100%)	21 (100%)	18 (86%)	21 (100%)
Healthy Controls	21	21 (100%)	21 (100%)	21 (100%)	21 (100%)	21 (100%)	20 (95%)	21 (100%)
TOTAL	82	81 (99%)	75 (91%)	78 (95%)	80 (98%)	81 (99%)	76 (93%)	80 (98%)

Evaluable defined as having contributed at least two out of three biofluids and two out of three biopsies

Continued from page 15

Results

S4 was able to recruit its full target population in a timely manner: 82 individuals were recruited to participate in S4 [Table 2] within 21 months. Although recruitment for the trial took three months longer than originally projected, the S4 Steering Committee considered this to be successful, particularly considering the harder-to-reach target population and complex protocol.

Conclusion

While a comprehensive site selection process may require a significant investment of time and resources at the outset, the benefits may outweigh the long-term risks (e.g., study delays, additional financial resources, high attrition rates, inability to meet enrollment goals).[8] Developing a checklist such as the one used by the S4 Steering Committee can facilitate the site selection process and lead to more open lines of communication between study sponsors and sites. Sites have an opportunity to share their interest, background and experience, and sponsors can dig deeper into questions they may have about the ways in which the protocol and operating objectives align.[9]

Chapter 2
Key Takeaways

+ Involve sites as stakeholders early in the study design process to help identify potential challenges and opportunities as they pertain to study feasibility and patient acceptability.

+ Use insights provided by sites and other stakeholders to identify and prioritize site characteristics.

+ Develop a template or questionnaire to facilitate site assessment and selection process.

[8] Harper, Beth and David Zuckerman. "Critical Success Factors for Planning for Planning for Site Selection and Patient Recruitment Planning." *BioExecutive International* (2006) pg.16
[9] Harper and Zuckerman, pg. 17

Chapter 3

Building a Recruitment Strategy and Toolkit

Objectives

+ Provide an overview of a recruitment committee and how it can be used to better understand your target population

+ Demonstrate how to craft messaging that is tailored to your target population and that will spur potential participants to action

+ Describe the importance of a multi-modal approach and how it can help you to engage with your target population

+ Illustrate how other research teams have enhanced their recruitment efforts through case studies

+ Present a toolkit of materials that can be used in the development of a recruitment strategy

+ Share an example of a Parkinson's disease trial that evaluated potential study sites for opportunities and challenges and incorporated this information into the site selection process

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The participant journey serves as a roadmap both for designing a clinical trial and for developing an effective recruitment strategy. In this chapter, we present a framework that builds upon insights from the participant journey and enables clinical trial teams to: 1) better understand their target population; 2) craft messaging that compels potential participants to action; and 3) engage participants through multi-modal methods of communication.

Clinical trial teams embarking on large, multicenter studies can use the steps outlined in this framework to develop a centralized and standardized recruitment strategy. This approach can help to reduce site-level burden while also expediting recruitment. Clinical trial teams involved in single-site or smaller scale studies can use this framework to guide development of outreach and recruitment materials. To complement and facilitate your strategy, this chapter also presents a toolkit of materials and examples of methods employed by other Parkinson's research teams to enhance their recruitment efforts.

Understand Your Target Population through a Recruitment Committee
(SP) (CR) (MC) (SC)

Forming a recruitment committee early in the planning phase of a clinical trial is fundamental to better understanding your target population and developing an effective strategy. This committee can take the lead on developing a set of centralized and standardized outreach materials to be distributed among your sites, helping to reduce burden and facilitate recruitment. It is important to include a diverse set of stakeholders on the committee, who will bring a variety of perspectives, cultural sensitivities and experiences with outreach to the discussion.

Objectives

The recruitment committee develops the recruitment strategy and communicates it to others. It creates messaging and standardized materials, talks to study leadership and to sites about the strategy and how it should be implemented, and fields questions or concerns as they arise. Additional objectives for the recruitment committee are to:

+ Guide study leadership on goals of the target population (i.e., what are their desired health outcomes, motivations to participate, perceived benefits from participating)

+ Provide insights regarding off-ramps (e.g., potential barriers to participation, frustrations with clinical research or study teams, challenges with current therapies)

+ Offer feedback on messaging (e.g., cultural sensitivities, vernacular, reading level) and the most effective methods for conducting outreach to the target population(s) (e.g., where do they get their information, how do they prefer to get their information, are they online)

+ Facilitate outreach among target audiences (e.g., do they have networks that they can engage to promote your study and how best to engage them)

+ Monitor recruitment strategies and adapt as necessary

Potential Members

Designate a member of the study's steering committee to lead the formation of a recruitment committee. The recruitment committee should include stakeholders from a number of different groups, but should not be so large that it becomes difficult to make decisions quickly and efficiently. An ideal number of participants in the recruitment committee is between eight and 12. For example:

+ Study principal investigators (1-2)

+ Study project manager (1)

+ Contract Research Organization project manager (1)

+ Clinical trial site representatives (e.g., site investigators or coordinators) (2-3)

+ Patients with Parkinson's disease and/or care partners (2-3)

+ Representatives of patient-facing or advocacy organizations (1-2)

+ Representatives of federal organizations or neurodegenerative disease associations (1)

+ Community clinician (e.g., movement disorder specialist, neurologist, primary care physician) (1)

To ensure your recruitment committee embodies a variety of perspectives, you may want to consider that patients and other community representatives have participated in clinical trials (or have other relevant experience) and are frequently engaged with lay audiences, through support groups or other

networks, so they are familiar with the perspective of those less fluent in scientific language.

When seeking out recruitment committee members, set up time for individual conversations to find out: 1) how much they know about the research; 2) if there is anything in particular that interests them about the study; 3) how active they are in their community; and 4) if there is anything they would want community members to know about this trial. (See "Sample Questions for Selecting a Recruitment Committee Participant Representative," on this page.) Asking these questions will provide you with insights into the perspective that potential members bring to the committee. Once you have had the opportunity to get to know potential members you should be able to determine what value they can add to the committee. Be highly selective in this process.

Recommended Organizational Structure

To enhance the efficiency of recruitment committee meetings, consider these tips:

+ Designate one person (typically the same study steering committee member who led formation of the recruitment committee) to facilitate regular meetings.

+ Hold monthly meetings to develop and review strategies, discuss study enrollment (projections and actuals) and propose solutions to any challenges or barriers.

+ Provide an agenda in advance of each meeting to allow members to solicit input from their networks and come prepared with thoughtful comments.

+ Summarize notes from each meeting and circulate to the group to create a historical record of the decision-making process.

+ Initiate recruitment committee meetings during the study planning phase and continue through study closeout.

An organized, efficient and thoughtful recruitment committee will not only make your job easier, it also will enhance your engagement with the community

and facilitate your recruitment efforts.

Sample Questions for Selecting a Recruitment Committee Participant Representative

These questions can guide conversations when selecting potential participant representatives for the recruitment committee.

+ If you had to explain our trial in three sentences, what would you say?

+ What are some examples of cultural sensitivities to science and clinical research?

 – Are there examples that are specific to this community?

+ What words associated with clinical research tend to scare or worry people?

 – Be prepared to provide examples if none are offered

+ If your loved one or significant other told you they were participating in this trial, what would your reaction be?

+ What are some words or phrases that would make you feel positively about a clinical trial?

+ What are some positive images that represent clinical trials?

 – It may be helpful to have a few examples on hand

+ What information would you need to know about a trial to be willing to participate?

+ What sensitivities around Parkinson's disease should be considered when talking about a trial?

+ How should patient-facing language differ from language used when describing the trial in the medical community?

+ How should the trial team discuss potential complications that could arise for patients and/or controls during this trial?

STEADY-PD III

Background

STEADY-PD III is an ongoing 36-month, double-blind, randomized, placebo-controlled study of isradipine in people with early Parkinson's disease (PD) who, at baseline, were not receiving symptomatic therapy or expected to require it for at least three months. The projected recruitment period was 18 months at 57 Parkinson Study Group sites across North America.

Methods

Participants and Procedures

STEADY-PD III aimed to enroll 336 men and women with early stage idiopathic PD. Participants had to be older than 30 at the time of diagnosis, diagnosed less than three years prior, and not receiving PD symptomatic therapy (e.g., levodopa, dopamine agonist or MAO-B inhibitor) or projected to require symptomatic therapy for at least three months from baseline visit. To participate in the study, eligible participants agreed to be followed for up to 36 months and complete 12 in-person visits and four telephone visits. The projected recruitment period was based on previously completed studies that targeted a similar PD population.

Forming a Recruitment Committee

Early in the planning process, the STEADY-PD III team identified and engaged key stakeholders from across the recruitment landscape to provide input on constituent motivations, knowledge gaps and outreach methods. This group, the recruitment committee, consisted of:

+ STEADY-PD III principal investigators

+ Site representatives (investigator and/or coordinator)

+ A representative from The Michael J. Fox Foundation (MJFF)

+ A representative from the National Institute of Neurological Disorders and Stroke (NINDS)

+ Patient advocates

The recruitment committee consulted with national Parkinson's disease organizations, including the National Parkinson Foundation (NPF) and the Parkinson Disease Foundation (PDF), which have since merged to form the Parkinson's Foundation. With this guidance, the committee developed a multi-modal recruitment strategy aimed at educating individuals in the PD community about STEADY-PD III and increasing awareness of resources related to the trial. This strategy was implemented through: 1) in-person meetings and events with community groups, physician networks and support groups; and 2) development of a heightened online presence using mixed media outlets. MJFF's Recruitment and Retention Toolkit materials, such as a "Health Care Provider Outreach Letter" and a "Patient-Facing Slide Deck," facilitated outreach efforts, as did grassroots peer engagement via MJFF's Fox Trial Finder Ambassadors, PDF's Parkinson's Advocates in Research (PAIR) and the Muhammad Ali Foundation's community leaders. A greater online presence was cultivated through: 1) creation of a study-specific website (steadypd3.com); 2) press releases (templates were provided in the Recruitment and Retention Toolkit) posted to websites such as NINDS; 3) use of Fox Trial Finder — MJFF's online trial matching service that enables volunteers to connect with trial teams (foxtrialfinder.org); and 4) webinars and podcasts hosted by the STEADY-PD III study principal investigators and broadcast to MJFF and NPF networks. Throughout the enrollment period the recruitment committee met monthly to review recruitment strategies, monitor enrollment at the study and site level, and identify challenges and solutions to any recruitment issues.

Results

A study enrollment report (Figure 1, opposite page), generated after all participants had been recruited, shows a steeper slope of actual vs. anticipated enrollment, reflecting a recruitment period accelerated by six months. In addition, the pre-specified goal of 10 percent minority recruitment was met. Analysis of MJFF communications that took place prior to and throughout the recruitment period provides insight into the role of mixed media in generating awareness of the trial, and directing individuals to resources for learning more about participation. In March 2014, MJFF, with study leadership, released a podcast that reported isradipine was moving to Phase III testing, and recruitment would begin later that same year. The podcast was downloaded by 2,043 iTunes listeners. This was followed by an uptick in traffic to the STEADY-PD III website (steadypd3.com) that began in May 2014 and peaked in July 2014 (Figure 2, pg. 22). One of the steepest peaks occurred in January 2015, after a December

2014 MJFF webinar that focused on therapies with the potential to slow or stop Parkinson's progression and highlighted the STEADY-PD III trial. A third peak took place in November 2015, after an October 2015 MJFF webinar and podcast on studies to slow or stop PD.

A multitude of subject referral sources bolstered STEADY-PD III recruitment success (Figure 3, pg. 22). Referral sources were recorded at the time of screening and logged into case report forms. These data indicate the top four referral sources were: site personnel (53.8 percent); neurologists (24 percent); Fox Trial Finder (10.2 percent); and MJFF communications (3.9 percent).

Discussion

By having a comprehensive recruitment plan and involving key stakeholders early in the planning phase of the clinical trial, STEADY-PD III was able to successfully recruit its full target population six months ahead of schedule. They identified study and site level barriers that had the potential to negatively impact recruitment, and were able to develop a strategy to mitigate them. One important component of that strategy was implementation of a comprehensive outreach and awareness campaign. Stakeholders such as PDF maximized peer-to-peer engagement via the PAIR program and local events including

the Brain and Health Fair and the Unity Walk; NPF harnessed the power of social media through webinars and press releases; MJFF leveraged technology such as Fox Trial Finder to connect volunteers to trial teams; and The Muhammad Ali Foundation increased participation of historically underrepresented minority populations with community engagement, translation of materials and outreach through the "Southwestern Parkinson's Newsletter." The use of local grassroots events and social media activities, combined with a proactive approach to recruitment, helped to engage and make aware a broader population than would have been possible for clinical trial sites alone. This approach also enabled study teams to connect with a more diverse population of patients who obtain their information from a variety of media and news sources. While the impact of these efforts is somewhat challenged by self-reported referral source data (Figure 3, pg.22), we posit that this is less about the efficacy of these efforts and more about challenges stemming from memory recall bias in referral source attribution. Greater efforts such as interviewer training, better referral source definition and alternative means of data collection should be considered for future recruitment campaigns to improve the accuracy of attribution.[10]

Figure 1. Actual vs. Projected Enrollment
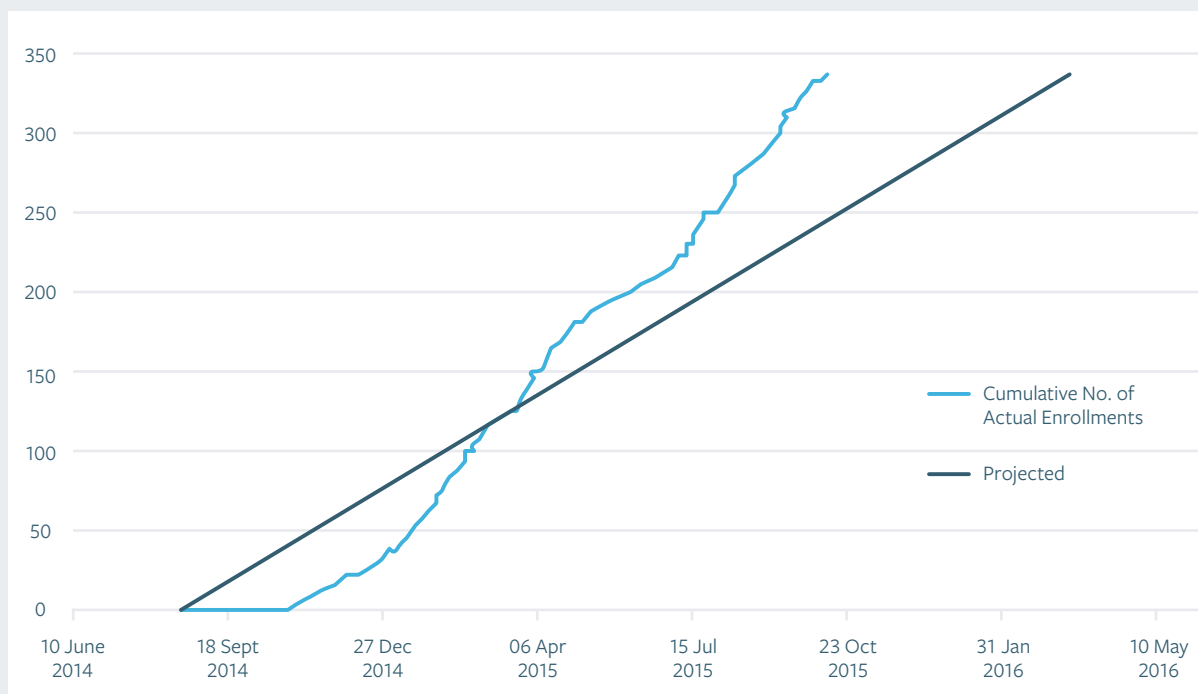
[10] *Hassan E (2005) Recall Bias can be a Threat to Retrospective and Prospective Research Designs. The Internet Journal of Epidemiology 3.*

Continued from page 21

Figure 2. STEADYPD3.com and MJFF Mixed Media Outreach
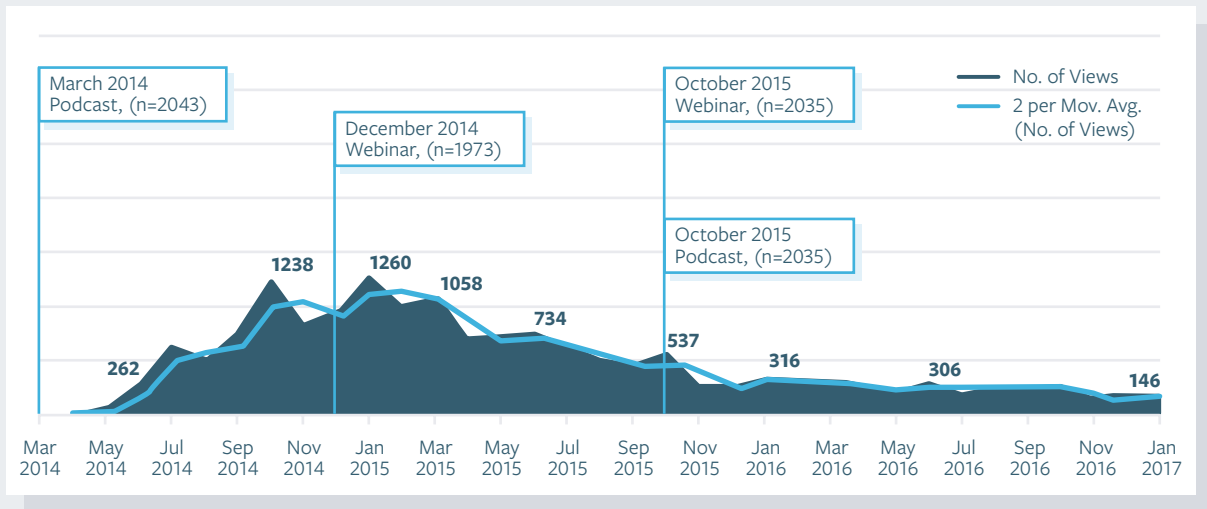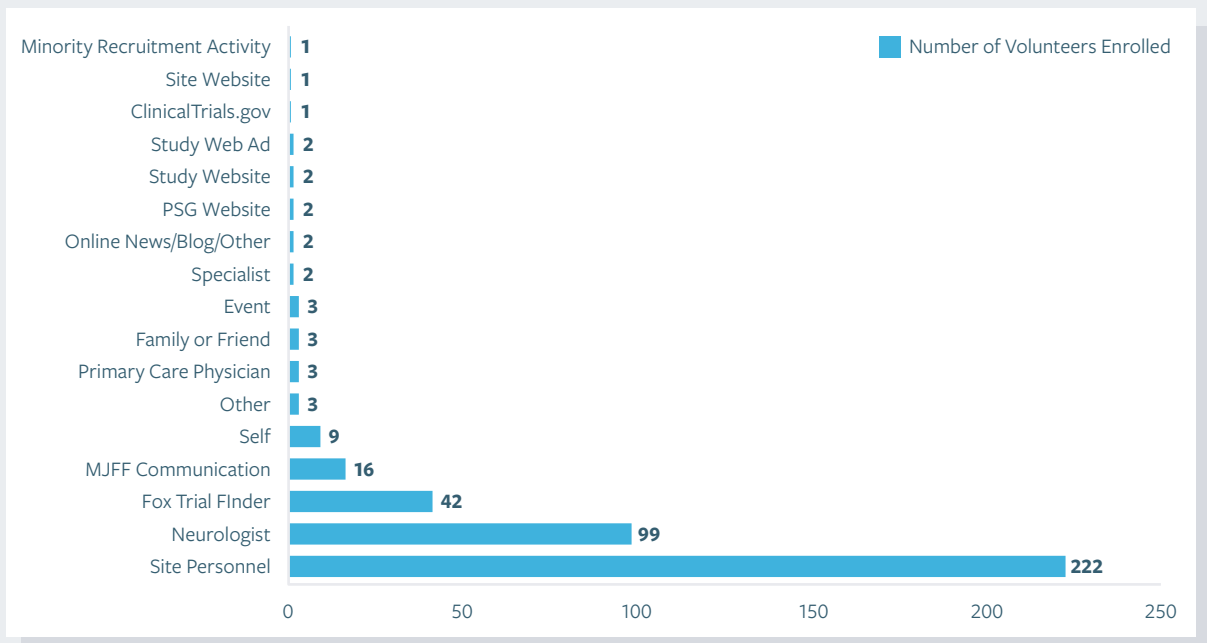

Figure 3. Referral Sources: Enrolled STEADY PD-III Volunteers

Conclusion

Involving stakeholders with a range of perspectives early on is important for learning about constituent motivations and barriers to participation. Taking this step at the beginning of a clinical trial can help in the formation of a comprehensive recruitment strategy allowing trial teams to reach a broader audience and more diverse target population.

For more information on the recruitment efforts used in the STEADY-PD III trial, visit: https://content.iospress.com/download/journal-of-parkinsons-disease/jpd171199?id=journal-of-parkinsons-disease%2Fjpd171199

Craft Messages That Compel Your Target Population

(SP) (CR) (MC) (SC)

A well-crafted message should consist of three key elements: content, purpose and a call to action (CTA). Frame the content of your message around the goals and off-ramps of the patient journey; your recruitment committee can establish these points. The purpose of your message speaks to how you are trying to change the perspective of your target population (e.g., make them aware, recognize them). The CTA prompts your audience to take next steps.

Content

Content focuses on the goals of potential participants and anticipates the off-ramps in the participant journey that may prevent them from completing a clinical trial. There are a number of nuances to consider within these categories. Frame these as questions for each target population that you are trying to engage.

+ Motivations: Do they want to speed research or find a cure, or is their behavior purely altruistic?

+ Challenges: Do they have significant motor or non-motor symptoms, transportation issues or communication difficulties?

+ Education level: Does language need to be simplified? Should content focus more on the science? Do terms need to be defined? Would analogies be helpful?

+ Cultural values: Do social norms support or oppose clinical research participation? If norms support research participation, what is the underlying rationale?

+ Language subtleties: Are there certain terms that should be included or avoided? Are there language differences across age or geographic location?

Purpose

The purpose of your message is the change in perspective you are prompting within your target population. Are you trying to:

+ Generate awareness of clinical research participation opportunities at your institution and/or ways that individuals can participate even if they don't meet the eligibility criteria for a specific study?

+ Educate potential volunteers about the importance of clinical research participation and the goals of your study?

+ Engage them as supporters of clinical research over the long term or as advocates to promote clinical research among peers?

+ Recognize them for their efforts and participation in research to advance science?

Call to Action

The call to action is what you would like your target population to do after they read your message. Some examples might include:

+ Participate in a specific trial at your institution or one of the participating sites

+ Visit a website to learn more about participation in your trial

+ Complete an online survey to share more about their daily experience with Parkinson's or to let you know how satisfied they were with participation in your trial

+ Share information with peers about a research opportunity or ways to get involved with research

An Educational Toolkit for Engaging the Hispanic Parkinson's Community

Background

Hispanics make up 17.6 percent of the U.S. population, and have become the largest ethnic minority in the country[11]. Yet they remain underrepresented in clinical research, constituting only one percent of study participants[12]. This figure is troubling, as a lack of diversity in clinical trials can lead to challenges validating the safety and tolerability of new therapies in broad populations.[13] Studies of clinical research participation in diseases other than Parkinson's (e.g., cancer, heart disease, diabetes), have attributed limited representation of Hispanics to barriers [14,15] such as:

+ Low awareness of clinical research opportunities

+ Language and cultural barriers

+ Financial or logistical challenges (e.g., lack of transportation to appointments, child care responsibilities)

+ Negative perceptions of research participation

Objectives

To explore whether Hispanic individuals in the Parkinson's disease (PD) community experience barriers similar to those with other diseases, Irene Litvan, MD, Tasch Endowed Professor in Parkinson's disease research at the University of California San Diego (UCSD), and her team designed and conducted a study called "An Educational Toolkit for Engaging the Hispanic Parkinson's Community," with these objectives:

+ Gain a better understanding of the knowledge, attitudes and perceptions toward research participation of individuals in the Hispanic PD community

+ Use insights to develop messaging for research materials for the Hispanic PD community

+ Incorporate messaging into an educational toolkit for the Hispanic PD community that is accessible, culturally sensitive, and available in English, Spanish and a combination of English and Spanish.

Method

Participants

To understand views on research participation from a variety of different perspectives in the Hispanic PD community, Dr. Litvan and team recruited individuals from the following key stakeholder groups:

+ Hispanic individuals with PD (n = 20)

+ Care partners of Hispanic individuals with PD (defined as people who spend at least three hours per day for three to four days a week with a PD patient, n = 20)

+ Physicians of primarily Hispanic PD patients (n = 6)

Materials

The UCSD team developed a flyer to facilitate recruitment of Hispanic individuals with PD and their care partners. An informed consent form to obtain verbal consent over the phone was created to make it easier for individuals to participate from their home or office [Table 1]. Interview guides were constructed to elicit qualitative data on attitudes, knowledge and experiences participating in PD clinical research from each key stakeholder group. (For more information on the materials used for this study, contact trialsupport@michaeljfox.org.)

Procedures

The UCSD study recruited Hispanic individuals with PD and their care partners via the UCSD electronic medical health record system and posted flyers throughout the USCD movement disorders clinic. Individuals who participated in the study received a $25 gift card. Physicians were recruited via the UCSD provider referral network. Physicians who participated in the study received a $100 gift card. All interviews were conducted over the phone using the interview guides, and participants notified the interviewer of their preferred language (i.e., English or Spanish). All interviews were recorded, transcribed and translated into English if conducted in Spanish. Qualitative analysis followed a phenomenological approach[16] (i.e., major themes were derived from the experiences

[11] https://www.census.gov/newsroom/facts-for-features/2016/cb16-ff16.html
[12] http://www.appliedclinicaltrialsonline.com/hispanics-remain-minority-clinical-trials
[13] http://www.appliedclinicaltrialsonline.com/hispanics-remain-minority-clinical-trials

[14] https://www.ahcmedia.com/articles/80723-overcoming-barriers-to-hispanic-participation-in-clinical-trials
[15] http://thenationshealth.aphapublications.org/content/43/7/1.2.full

and perspectives of interviewees). All data were analyzed using the qualitative analysis software QDA Miner (For more information, visit provalisresearch.com.)*

Results
Six major themes emerged from the initial results. Table 1 describes these themes in detail.

Discussion
Initial findings provide insight into the barriers that can be addressed when engaging with individuals in the Hispanic PD community. As with other diseases, limited knowledge and awareness of clinical research opportunities for Hispanic people with PD is a challenge. This is perpetuated by a lack of locally available educational materials in Spanish, requiring individuals in the Hispanic PD community to go to greater lengths to seek information, such as from Spanish-speaking countries, like Spain or Mexico, to learn more about Parkinson's disease and clinical research. Physicians underscored this finding, noting they have limited materials in Spanish for communicating with both patients and the larger community about Parkinson's disease and research.

The research also pointed to a few facilitators for engaging with individuals in the Hispanic PD community. Certain stakeholders, such as family members, care partners and physicians are a critical conduit of information, and should be involved in any engagement or recruitment strategy. Family members in particular play crucial roles in making decisions about care and treatment, as well as research participation. Materials should be tailored to enable discussion about research participation among family members. A somewhat surprising finding, and potential facilitator, is the number of individuals in the Hispanic PD community who experience comorbidities, such as diabetes, and are therefore familiar with clinical research because of these comorbidities. Collaborating with disease-focused advocacy groups that already engage individuals in the Hispanic community might serve as a point of entry for involving the Hispanic community in PD research.

Future Directions
The UCSD study findings will be finalized and incorporated into an educational material toolkit. These materials will be available in English, Spanish and a combination of English and Spanish, and will be offered on The Michael J. Fox Foundation website in Fall 2018. (For additional information on this toolkit and how you can use it in your research, contact trialsupport@michaeljfox.org.)

Table 1

Theme	Overview
Pre-diagnosis and Diagnosis	Explores the initial physical and emotional journey that a patient undergoes when recognizing PD symptoms and seeking a diagnosis
PD Care	Looks at the second leg of the patient journey with PD, specifically the learning curve with medications (adherence and optimization)
Living with PD	Examines changes that have occurred in individuals' lives after a PD diagnosis and how they talk about living with PD
Role of Family and Care Partner	Provides insight into the ways in which family and care partners are gatekeepers of information and play a large role in decisions about care and treatment, including research participation
PD Knowledge	Highlights various resources that individuals use to learn more about PD, different information-seeking behaviors and barriers that individuals experience when trying to learn more about research; attitudes, values and motivations around research participation
Research Engagement	Dives deeper into specific barriers and facilitators to research participation

*https://provalisresearch.com/products/qualitative-data-analysis-software/freeware/
[16] https://www.capilanou.ca/psychology/student-resources/research-guidelines/Phenomenological-Research-Guidelines/

Use Multiple Communication Methods to Engage Your Audience
(SP) (CR) (MC) (SC)

The recruitment committee can help you identify a series of touchpoints that your target population will experience throughout the patient journey. These may include personal interactions with clinicians and support groups, or digital engagement through platforms such as Fox Trial Finder (foxtrialfinder.org). Think about how best to communicate with your target population at these touchpoints. For example:

+ Create a study website that serves as a clearinghouse of information about participation in your trial

+ Obtain a toll-free telephone number for your study that can be posted on your website or printed on outreach materials, so that individuals can call for information and ask questions

+ Post flyers or educational materials in the office of a neurologist or movement disorder specialist

+ Conduct outreach at your clinic using pamphlets, talking points and other educational materials

+ Leverage electronic health records and electronic databases managed by your institution

+ Present information on your trial and ways to get involved in research at support groups and primary care clinics using educational slide decks

+ Create a trial posting on Fox Trial Finder, The Michael J. Fox Foundation's online clinical trial matching tool.

+ Promote your trial via advocacy and patient-facing organizations using websites, newsletters, webinars, podcasts or blogs

+ Send emails, newsletters and blogs about your trial to your network listserv or to network listservs of community organizations and patient advocacy organizations

+ Host webinars featuring study leadership to help individuals learn more about your trial and trial team members

Once you and the recruitment committee have generated a list of the top three or four methods to reach your target population (base the number of methods you select on available bandwidth and resources), you can begin to flesh out your recruitment strategy. This strategy should include a timeline with milestones for different methods of engagement, as well as the number and type of messages that you will use with each. The timeline for your recruitment strategy should correspond with the projected enrollment period. If possible, track the number of referrals and/or inquiries that you receive from each method of engagement. This will help you to determine which of these strategies was most effective and which was least effective in recruitment and where efforts should be concentrated.

Institute for Neurodegenerative Disorders Physician Referral Network

Physicians play a critical role in facilitating patient participation in clinical research.[17] In fact, a poll by Research!America found that 72 percent of respondents would participate in a trial if their doctor recommended it.[18] However, primary care physicians and neurologists often are not involved in the recruitment strategy for clinical trials. Historical barriers have made engagement with physicians challenging. They may fear losing care of patients to clinical trial site providers, be unfamiliar with the trial and principal investigator, or have concerns about jeopardizing the doctor-patient relationship.[19,20] One approach to building trust and overcoming these obstacles is for research institutions and principal investigators to actively engage with community physicians. Reaching out to local physicians to increase knowledge about trials and generate confidence can facilitate referrals.

The Institute for Neurodegenerative Disorders (IND) serves as a prime example of how research institutions can better engage with community physicians to build referral networks. Founded in New Haven, Connecticut, in 2001, IND develops diagnostic tools and treatments for individuals with neurodegenerative disorders. Its founders, Kenneth Marek, MD, and John Seibyl, MD, bucked the traditional research institution model. Foregoing regular clinic hours, they focused instead entirely on clinical research studies. This novel approach meant that trials conducted at IND had to rely heavily on patient referrals from community clinicians. Through several years of dedicated outreach to clinicians in the community, IND built a referral network of neurologists located across the state of Connecticut. As a result, the top two referral sources for trials at IND are: 1) new patient referrals from community clinicians, and 2) a database of patients referred to past IND studies. This resource of patient referrals has made IND a top recruiting site for Parkinson's studies, including the Parkinson's Progression Marker Initiative (ppmi-info.org).

The Institute of Neurodegenerative Disorders may seem uniquely positioned for success in the development of a physician referral network, but Director of Clinical Research David S. Russell, MD, PhD, believes that traditional research institutions can easily replicate these efforts. Dr. Russell outlines a three-tiered strategy to facilitate engagement and long-term relationship building among community physicians:

+ **Conduct Due Diligence**

  – **Learn about the practices in your community.** To maximize your time and effort, do online research about local practices. Begin with neurology clinics that see individuals with Parkinson's disease (PD). Identify a neurologist, physician assistant or nurse practitioner who regularly treats PD patients. Consider connecting with primary care physicians and allied health care professionals, but prioritize neurologists as they more frequently engage with PD patients. For IND, neurologists historically have provided the most referrals.

  – **Understand the needs of community clinicians.** Ask physicians about challenges they may be facing in their practices. For example, a community neurologist may be having difficulties diagnosing a patient. Offer to provide an expert second opinion and send your recommendations. Point out research studies that include procedures and assessments that physicians may find useful to treat their patients. For instance, Dr. Russell has found that community physicians often seek DaTscans for their patients. In addition, explain the various patient wellness programs available at your site, such as support groups, PD education events and fitness classes. Patients can learn about recruiting trials at your site through these programs.

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[17] *http://www.appliedclinicaltrialsonline.com/print/343713?page=full*

[18] *https://www.elsevier.com/connect/poll-majority-of-americans-would-participate-in-clinical-trials-if-recommended-by-doctor*

[19] *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3782313/*

[20] *Michaels, Margo, et al. "Impact of Primary Care Provider Knowledge, Attitudes, and Beliefs about Cancer Clinical Trials: Implications for Referral, Education and Advocacy." Journal of Cancer Education, vol. 30, no. 1, 2015, pp. 152-157, Research Library,*

Continued from page 27

– **Explain the value of research.** In addition to sharing the latest in PD research and recruiting trials, remind community physicians that these studies are necessary for the discovery of PD biomarkers and new and improved treatments. Physicians want the best care for their patients. Reminding them of the importance of clinical research in this process may motivate them to provide referrals. Explain that clinical trials give patients treatment options and access to certain procedures, such as a DaTscan, at no cost.

+ **Build Relationships**

– **Be willing to dedicate time.** Developing a partnership with community physicians cannot be done overnight. It took years for IND to forge the relationships it has today. At the outset of building a referral network, remember it will take time and effort to be successful.

– **Schedule a face-to-face meeting.** When trying to engage with community clinicians, there is no substitute for a face-to-face meeting. Begin by calling the practices you have identified. Introduce yourself, provide them with background on your research, and let them know that you are trying to generate awareness about PD studies at your institution. Invite the clinician(s) to your office for a discussion with other medical providers from the community about the latest advances in PD research and any trials that are currently recruiting. Maximize your time and the number of physicians you can connect with by hosting the meeting in your office or another location that can accommodate a bigger group. If a physician rejects the invitation, be persistent and ask for times that you can drop by their office.

– **Facilitate patient referrals.** Make the process of referring patients as simple as possible. Give local practices study flyers and brochures for patients to read in the waiting room and discuss with their doctor. Provide physicians with pocket cards listing high-level eligibility criteria to quickly reference when examining patients. Avoid presenting community clinicians with eligibility criteria not usually gathered through standard clinical care, such as scales and questionnaires used in clinical trials. Physicians may rule out patients if they do not know all the eligibility criteria. Supply practices with a fax referral form to easily send contact information and a note about interested patients. Obtain patients' contact information,

with their permission; this is faster and more efficient than waiting for patients to call the research site. (For more information, visit ppmi-info.org.)

+ **Engage with Physicians for the Long Term**

– **Build trust.** Assure community clinicians that your intention is to expand awareness about research opportunities and help interested patients find a study that is right for them. To alleviate fears that they may lose patients to health care providers at your institution consider the following language: "We will provide only the care necessary to conduct the trial and to ensure patient safety. We will refer the patient back to you for any clinical issues."

– **Communicate patient progress.** Update referring clinicians about their patients on a regular basis. If a patient is not eligible for any recruiting studies at the site, send the referring physician a note expressing your gratitude for the referral and explain why the individual was ineligible. If a referred patient is a study candidate, inform their doctor and make yourself available to answer questions. Upon enrolling a referred patient in a study, send their physician a letter explaining any medical precautions or exclusionary medications. After a patient is enrolled, provide the referring physicians with updates around milestones such as a patient's test results, study withdrawal and/or completion. Consider organizing a group meeting or webinar to explain study results to all referring physicians.

– **Reinvigorate your physician referral network.** Building a referral network is an ongoing process. Physicians leave practices and new ones are added. It is important to develop new partnerships and maintain existing relationships. IND invites community clinicians from across the state of Connecticut to dinner twice a year to discuss advances in PD research and new treatments or challenges in the field. A biannual webinar also can serve as an alternative to an in-person meeting. Remember to express gratitude to physicians in your network for their continued commitment to advancing Parkinson's research.

While there is no denying that building a physician referral network takes time and dedication, expanding research awareness to more clinicians and ultimately more patients can help accelerate recruitment for clinical trials. (For more information on the Institute for Neurodegenerative Disorders and their work, visit indd.org.)

A Recruitment Toolkit to Facilitate Engagement

(SP) (CR) (MC) (SC)

With a more thorough understanding of your target population, compelling messages and methods for engagement, it is time to put it all together into one cohesive package. To facilitate this process, The Michael J. Fox Foundation has created a Recruitment and Retention Toolkit containing educational materials, customizable templates and how-to guides. Of these tools and resources, some materials are patient-facing (i.e., research teams will distribute them to individuals with Parkinson's and/or their care partners) and others are trial team-facing (i.e., internal to and only used by trial teams). The majority of toolkit materials are customizable templates into which you can enter compelling messages and study-specific information. The templates are designed with placeholders for study-specific branding. Once you have selected the templates that best fit the needs of your recruitment strategy, create a toolkit that can be used at your site or distributed if you are part of a multicenter study. (Additional information on the Recruitment and Retention Toolkit can be found at michaeljfox.org/ResourcePack.)

Digital and Online Recruitment Resources

(SP) (CR) (MC) (SC)

Digital marketing — the use of online channels to advertise a product or service — is another tool that clinical trial teams can and should use to broaden the pool of potential participants, track recruitment efforts and reduce site burden. Using online resources to engage and recruit trial participants can help increase efficiency and lower costs. There are two main approaches to digital marketing: paid marketing and organic marketing. Paid marketing is the exchange of money to advertise your trial or service (e.g., a banner ad that pops up on someone's Google homepage), whereas organic marketing is free advertising of your product or service (e.g., a LinkedIn post by an employee of your organization). If you have never engaged in a digital marketing strategy, it might seem a little intimidating, but we have compiled a guidebook in the Recruitment and Retention Toolkit that provides an overview of digital marketing and helpful resources to get you started. (For additional support in the development of a marketing strategy for your trial or study, email trialsupport@michaeljfox.org.)

The Michael J. Fox Foundation's Recruitment and Retention Toolkit

| Educate on Research Participation | Generate Study Awareness | Guide Through Consent | Facilitate Participation | Communicate Progress & Appreciate Participants | Share Study Results |

Learn more at
michaeljfox.org/ResourcePack

Using Facebook Ads to Recruit Study Participants

Background and Objectives

With 80 percent of individuals going online to learn more about specific diseases or treatments, digital media has become a leading source of health information.[21] More and more, people use mobile devices to find this information, making it easier to gather consumer demographics, such as age, gender and location.[22] This growing population of online users represents an opportunity for clinical researchers to engage with and recruit a broader audience at a lower cost than through traditional marketing channels.

To determine the efficacy of digital marketing as a low cost method of recruitment, The Michael J. Fox Foundation (MJFF), in conjunction with the Fox Insight Recruitment Committee, designed a marketing pilot to recruit individuals with late-stage Parkinson's disease (PD) to Fox Insight. Fox Insight (foxinsight.org) is MJFF's online longitudinal study that collects patient reported outcomes on the daily lived experience of individuals with and without PD. Objectives for the marketing pilot were to: 1) increase the volume of enrolled participants through Facebook advertising; 2) target and enroll participants at specific stages of disease; and 3) examine costs of recruitment using digital methods.

Methods

Participants

To ensure that Fox Insight accurately captures the daily lived experience of Parkinson's disease, it is imperative that individuals at different stages of disease are equally represented in the study. However, age, and motor and non-motor symptoms make it challenging for individuals with later-stage PD[23, 24, 25] to participate in clinical research, and often they are underrepresented. People with late-stage PD were an important target population for the marketing pilot. To be shown an ad, individuals had to meet the following eligibility criteria:

+ Currently living in the United States

+ Age 60 or older

+ Indicated "Parkinson's disease awareness" as an individual interest and selected interests in subject areas related to PD or clinical trials (e.g., clinical trials, PD symptoms and PD organizations) on Facebook

+ Not already involved in the MJFF online community (e.g., had not visited the MJFF website in the past 30 days and had not ever "liked" the MJFF Facebook page)

Facebook was selected as the platform for the marketing pilot because of its vast reach, many targeting capabilities,[26] and tracking techniques that enabled referral source attribution for those individuals recruited to Fox Insight.

Materials

Two types of Facebook ads were designed for the marketing pilot. One was aimed at individuals ("me" language) and the other emphasized the collective effort of clinical research ("we" language). Two subthemes were tested for each type of ad.

+ Individual (me): Language appealed to users on an individual level, to be empowered to impact research by participating in an online clinical study (Fox Insight). An image of an individual participating in Fox Insight on their computer accompanied these ad variations.

  – Subtheme: Research Reimagined (Figure 1, opposite page)
  – Subtheme: Lead the way (Figure 2, opposite page)

+ Collective (we): Language encouraged the user to contribute to a larger cause by participating in an online clinical study (Fox Insight). An image of a family sitting together in a waiting room accompanied these ad variations.

  – Subtheme: Join a Collective Goal (Figure 3, page 32)
  – Subtheme: Impact the Future (Figure 4, page 32)

[21] http://www.pewinternet.org/2011/05/12/the-social-life-of-health-information-2011/
[22] https://www.mdconnectinc.com/medical-marketing-insights/2016-trends-for-digital-recruitment-in-clinical-trials
[23] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2695395/
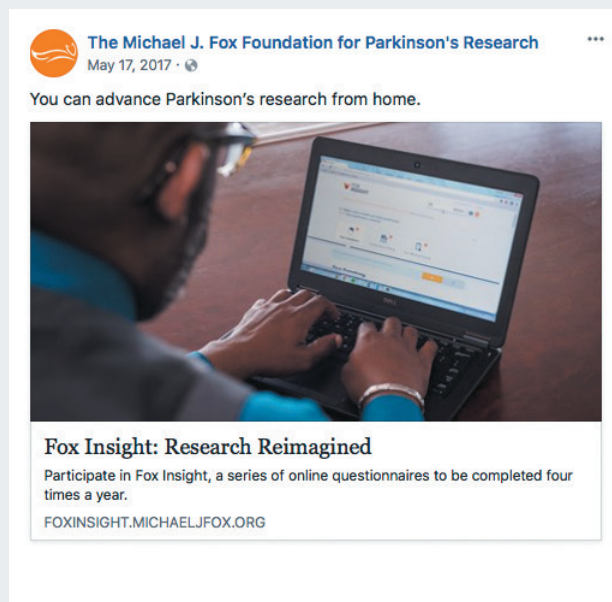[24] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3038575/
[25] (defined as having been diagnosed for ≥ 10 years, a score of 25 or higher on the MDS-UPDRS (Part II) and an NMS quest score of 13 or higher)
[26] https://www.mdconnectinc.com/medical-marketing-insights/digital-marketing-lowers-clinical-trial-recruitment-costs

Figure 1

Figure 2

Design and Procedures

The different ad variations were tested in three phases over a period of six weeks. Each phase cost approximately $8,000. At the end of each phase, the number of individuals recruited to Fox Insight along with the cost per recruit was evaluated.

Phase 1
+ Timing: Weeks one and two; ads shown approximately twice a day
+ Variables tested: Compared the efficacy of the four different ad variations to determine if users were more responsive to language/image combinations that fell in the individual or the collective categories, and within these categories, which messaging was most effective.

Phase 2
+ Timing: Weeks three and four; ads shown approximately twice a day
+ Variables tested: Compared levels of responsiveness to the winning ad variation from phase 1 among individuals with different Facebook interests. The two interest groups that were compared were: 1) individuals with interests in Parkinson's disease awareness and terms related to PD symptoms individuals with interests in Parkinson's disease awareness and terms related to clinical research. The two interest groups were mutually exclusive. Interest targeting is made possible on Facebook by the information that individuals add to their timeline, keywords associated with pages they like, apps they use or ads they have clicked on.

Phase 3
+ Timing: Weeks five and six; ads shown approximately twice a day
+ Variables tested: Assessed the efficacy of the winning ad variation from Phase 1 among a broad target audience without any interests defined.

Study enrollment after each phase of marketing pilots was compared to baseline (a six week period, pre-intervention) where no special promotion of Fox Insight took place, and recruitment was only facilitated through MJFF educational content and Fox Trial Finder.

Figure 3

Figure 4

Results

Total Enrollment

The marketing pilot significantly increased (825 percent) participant enrollment compared with baseline in terms of overall participants, individuals with PD and controls. During the pilot, a total of 1,138 participants, 46 percent of whom were individuals with PD, enrolled in Fox Insight. Of the 1,138 participants that enrolled in Fox Insight, 760 came directly from Facebook.

Population-Specific Targeting

The Fox Insight Facebook Ads Campaign recruited to the trial (Chart 1):

+ 23 individuals with PD with a score of 25 or higher on the MDS-UPDRS (Part II)

+ 64 participants with a PD diagnosis of 10 or more years

+ 93 individuals with PD with a Non-motor Symptoms Questionnaire (NMS quest) score of 13 or higher

Recruitment Costs

The cost per conversion (i.e. the total cost of advertising/number of enrollees) of those individuals who came directly from Facebook (n=760) was $31.51/per enrollee.

Chart 1

A bar chart titled with y-axis labeled "Number of Participants Recruited" ranging from 0 to 100. Three bars: MDS-UPDRS 25+ = 23, PD Diagnosis 10+ yrs = 64, NMSQuest 13+ = 93.
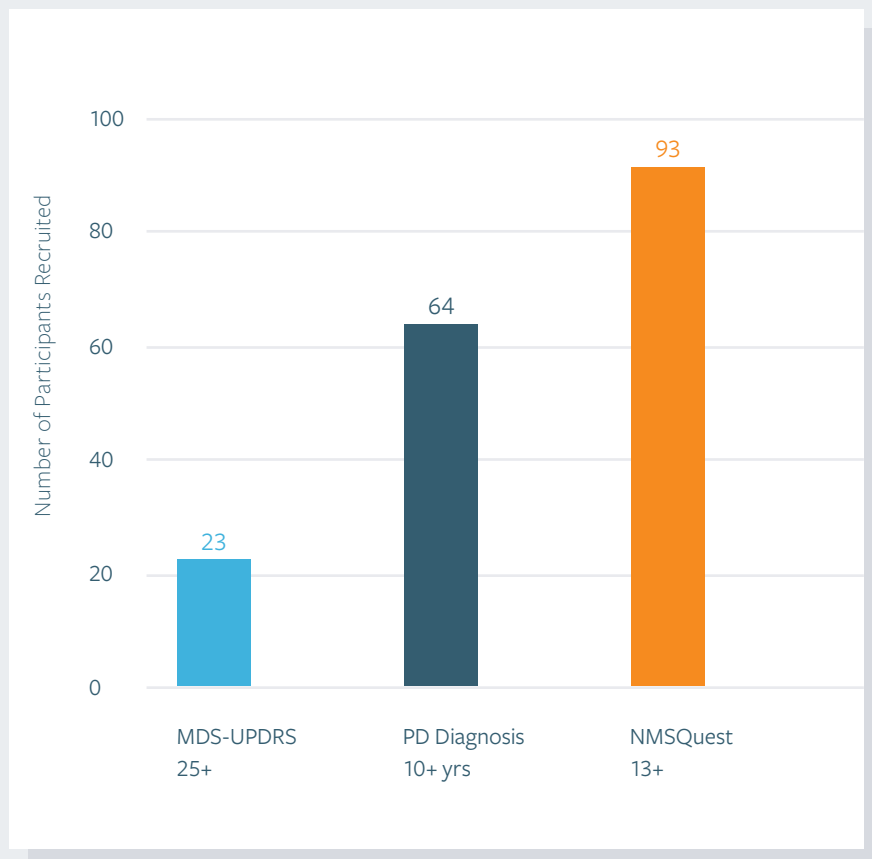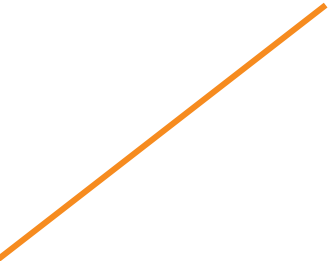
Discussion and Conclusion

Digital marketing is an effective outreach tool with substantial capacity to increase the number of research participants in Fox Insight compared to organic recruitment through MJFF educational content and Fox Trial Finder. This Facebook campaign was particularly successful for enrolling individuals with late-stage PD. Results also indicate potential applications for recruiting individuals from diverse racial and socioeconomic backgrounds, and for driving broad populations of prospective participants from digital advertisements to online study resources. Given the success of targeting a specific subset of the PD population through this pilot, MJFF will explore other applications of targeting and enrolling different subsets based on geography, socioeconomic status and additional characteristics to better reflect PD epidemiology and to diversify the demographic composition of participants in research.

Chapter 3
Key Takeaways

+ Form a recruitment committee early in the planning phase of your trial to understand goals, off-ramps and touchpoints for your target population.

+ Craft compelling messages that spur your target population to action by considering content, purpose and a call to action.

+ Work with your recruitment committee to determine the most effective methods for engaging your target population. Create a recruitment strategy that incorporates your messaging and outlines how and when you will deploy it.

+ Use MJFF's Recruitment and Retention Toolkit to consolidate your recruitment strategy into a cohesive package for your sites.

FOX TRIAL FINDER
THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

Fox Trial Finder is an online clinical trial matching platform that was created by The Michael J. Fox Foundation to help increase the flow of willing participants — both people with Parkinson's and control participants who do not have Parkinson's — into the clinical trials that need them, accelerating the Parkinson's drug development process.

Fox Trial Finder (foxtrialfinder.org) not only lists ongoing PD and atypical parkinsonism clinical trials and studies, but also matches registrants to the recruiting trials that are best-suited to their specific traits. Fox Trial Finder has a secure and anonymous messaging system, making it easy to find and act on opportunities to get involved.

Fox Trial Finder's algorithm identifies possible volunteer matches for your trial based on several key criteria. When volunteers create a profile on Fox Trial Finder, they provide data points such as age, gender, medication history, time since diagnosis, location and willingness to travel. When trials are posted to the site, the tool can quickly compare these data points with a trial's participation criteria and identify volunteers in the system who may qualify to enroll.

Overall trial coordinators for each trial ("trial leads") can register themselves to edit trial details as well as assign ownership of specific sites to site coordinators ("site owners") on Fox Trial Finder.

This empowers trial leads to oversee recruitment for the entire trial while empowering site owners to manage and engage with matches in their area. When a new volunteer is a match for a specific trial and location, Fox Trial Finder automatically alerts both the site owner and the volunteer about the possible match. From here, site owners can further explore the potential match by reviewing additional basic information about the volunteer in the volunteer's de-identified profile and, if appropriate, follow up by sending the volunteer a message. To register your trial and create a team profile on Fox Trial Finder, visit foxtrialfinder.org. For guidance on ways to maximize your Fox Trial Finder experience, visit michaeljfox.org/ResourcePack where you can find the following materials:

+ **Getting Started on Fox Trial Finder**
+ **Fox Trial Finder for Trial Teams**
+ **Fox Trial Finder Posting Template**
+ **Fox Trial Finder Message Template**

Chapter 4

Crafting a Retention Strategy and Toolkit

Objectives

+ Define the four elements of a retention strategy

+ Explore how these elements can be applied to a clinical trial

+ Present a toolkit of materials to facilitate the process of creating a retention strategy

+ Examine the Parkinson's Progression Marker Initiative as a case study of ways to successfully incorporate a retention strategy

Enrollment represents only the beginning of the participant journey. Most of an individual's experience with a trial takes place afterward. Therefore it is critical to put measures into place to ensure a positive experience for participants, and the site staff taking care of them, throughout the remainder of their journey. One way to achieve this is to develop a retention strategy early in the clinical trial planning phase. A strong retention strategy consists of four elements: 1) facilitate participation; 2) communicate study progress; 3) express appreciation; and 4) share study results. The process of creating a retention strategy also brings to light potential sources of attrition, which can increase study costs and reduce the validity of results. By anticipating these off-ramps, you can take steps to mitigate them.

Understand Study Participants through a Retention Committee
(SP) (CR) (MC) (SC)

Developing a retention strategy should go hand-in-hand with developing a recruitment strategy early in clinical trial planning. Select a retention committee to direct the process. Designating recruitment committee members to lead the retention committee will enhance the consistency of the strategic development process while also saving time and effort for all involved. The role of a retention committee is similar to that of a recruitment committee: to determine the motivations and off-ramps of study participants and to identify important touchpoints for communication post-enrollment.

Objectives

+ Guide study leadership on participant motivations (e.g., more time with a physician, additional information on their diagnosis, extra education on the research topic or appreciation for their participation)

+ Provide insights about off-ramps (e.g., remembering to take the study drug or complete diary entries, anxiety about a procedure, travel burden, not getting study updates, not feeling a sense of community, confusion on appointment dates or not feeling appreciated)

+ Facilitate communication and information sharing with study participants and site staff (e.g., host webinars, distribute quarterly newsletter, host quarterly calls to provide updates on study progress)

Recommended Organizational Structure

To enhance the efficiency of retention committee meetings, consider these tips:

+ Assign one or two members from the recruitment committee to lead the retention committee and develop a retention strategy.

+ Convene monthly meetings to provide updates and discuss retention rates, challenges with attrition and proposed solutions to keep participants engaged.

+ Begin retention committee meetings during the study planning phase and continue through study closeout; retention should be the sole focus of monthly meetings once enrollment is complete.

Create a Retention Strategy and Toolkit
(SP) (CR) (MC) (SC)

An effective retention strategy is aimed at both study participants and study staff. Many trials last longer than a year, and individuals can lose sight of study objectives, encounter challenges to participation or become disengaged. These risks make it imperative to develop a comprehensive retention strategy early in the trial. The retention strategy should incorporate the goals, off-ramps and touchpoints identified by the retention committee, and work to: 1) facilitate participation; 2) communicate study progress; 3) express appreciation; and 4) share study results.

+ **Facilitate participation:** An individual's life does not stop once they enroll in a clinical trial. They may move, experience a major life event or start a new medication. Be as accommodating as possible to any challenges or changes that may arise. Develop systems to remind patients of upcoming appointments and/or provide them with scheduling tools, such as a calendar of events. Give them materials to facilitate conversations about the study with their physicians and loved ones so they can more easily obtain the support they need to participate. A patient satisfaction survey is another helpful tool that can be used to better understand aspects of the trial that participants enjoy and those that could be improved. (To view and download an example of a satisfaction survey created by the Foundation, visit michaeljfox.org/ResourcePack.) Offering transportation support also is a great way to make participants feel valued and to lessen the stress of coordinating rides for appointments.

+ **Communicate study progress:** Remind study participants and site staff that they are involved in a trial that could advance the state of Parkinson's disease research. This

helps to contextualize the importance of the time and energy that they are putting forth. Sharing progress on major study milestones, such as completing enrollment, as well as any preliminary findings or procedure updates will go a long way toward enhancing and facilitating engagement. You can achieve this by hosting study webinars, distributing a quarterly newsletter (one for participants and one for study staff) or posting updates to a study website.

+ **Express appreciation:** One of the most critical components of the retention strategy is to let site staff and study participants know how grateful you are for their involvement. During the planning phase, the retention committee should think through and identify milestones at which to demonstrate a token of appreciation. These might include completion of participant's first study visit, conclusion of study enrollment or holidays (e.g., birthdays, Halloween, New Year's). Expressions of gratitude can take the form of thank-you cards, coffee mugs or other memorabilia that serve as a reminder of their contribution.

+ **Share study results:** Once study analyses have been completed, let site staff and study participants know how and when they can learn about trial results. If possible, post links to any webinars or publications on your study website. Sharing these results with participants is a way to create long-term community engagement and shows individuals how their contributions advanced research. Even if the results are not positive, helping participants understand the lessons that were learned from their involvement is invaluable. Remember the following ethical and logistical factors as you prepare to share study results:

  – **Outline a communication plan in your study protocol:** After consultation with a central Institutional Review Board (IRB), create a strategy for communicating study results to participants that includes how the results will be shared (e.g., via letter, webinar or newsletter).

– **Make a commitment to share study results:** Although it may take several years from the start of a study for results to be available, study teams must be determined to share results with all participants and develop a plan to do so.

– **Consult an ethical review board:** Speak with an ethical review board member about what is required to share results with participants after study completion and plan accordingly.

– **Request permission for future communication:** The study's informed consent document should ask participants for their contact information, including email address, and consent to be contacted about study results. Consult your IRB regarding appropriate language for the consent form.

– **Develop materials to share results:** Decide between individual or mass communication of study results. Use letters or email for individual communication. For mass communication, consider hosting a webinar or posting on a study website. Even if you choose mass communication, create an individual letter, email or phone script to inform participants about the webinar date or publication of results on a website. Although results may not be available for some time, submit the communication materials and strategy to the IRB for approval prior to study closure. Doing so will ensure timely distribution of findings once available.

– **Confirm contact information:** For individuals who agreed to be contacted in the future regarding study results, ensure that contact information is up-to-date at the last study visit. Create a secure document to house and easily access this information when study results are available

Retention Strategies for the Parkinson's Progression Markers Initiative

To complete a study, it is critical to retain study participants. Participant attrition has the potential to interfere with the scientific validity of the study and distort data designed to measure drug efficacy and safety. According to Forte Research:[27]

+ Eighty-five percent of clinical trials fail to retain enough participants

+ The average dropout rate across all clinical trials is 30 percent

Retention is an important element of the Parkinson's Progression Markers Initiative (PPMI), a landmark, longitudinal, observational study sponsored by The Michael J. Fox Foundation. PPMI (ppmi-info.org) aims to find reliable and consistent biomarkers for Parkinson's disease (PD) progression by studying cohorts of Parkinson's patients (de novo idiopathic PD and PD-manifesting genetic mutation carriers), populations at risk for PD (non-manifesting genetic mutation carriers and subjects at risk due to REM sleep behavior disorder or hyposmia) and controls without PD. Participants in PPMI commit to long-term participation, providing biospecimens (e.g., blood, urine, spinal fluid), and undergoing multiple neuroimaging, clinical and behavioral procedures, and assessments over a period of at least five years. The study launched in 2010, and since that time, approximately 1,500 individuals have enrolled. PPMI's retention rate has consistently held strong, year after year, at about 90 percent.

To ensure steady participation and to prevent attrition, PPMI weaves together four key tenets of retention, cultivated and refined since study launch: 1) facilitate participation; 2) communicate study progress; 3) express appreciation; and 4) inform participants of study results.

+ Facilitate participation through travel concierge services: PPMI study leadership prioritized and simplified long-term participation in large part because individuals carrying specific PD-linked genetic mutations live across a wide geographical area. To facilitate volunteers' continued participation, PPMI cultivated a boutique experience for them and their care partners. Prospective and enrolled PPMI participants are given the option for complimentary round-trip transportation between their home and appointments at two "super sites" that have the capacity to handle a high volume of study volunteers. A third-party vendor manages all logistical planning, including participants' accommodations, meals, and travel to and from study visits. This door-to-door service reflects the value PPMI study leadership puts on participation and participants.

+ Communicate study progress through newsletters, update calls and a centralized webpage: Reminding participants of the bigger picture is a meaningful way to engage them in the collective success of a study. According to a 2017 report by The Center for Information and Study on Clinical Research Participation,[28] the number one reason individuals choose to participate in clinical research is to help advance science or the treatment of a disease or condition. Given this initial motivation, updates on study progress and contributions to the field will facilitate continued engagement. In PPMI, study progress is communicated in several ways:

– PPMI newsletters provide high-level updates on the study (e.g., study enrollment progress, how the data and samples collected are being used for research) as well as interviews or profiles of study participants and/or study staff.

– PPMI update calls, which are scheduled throughout the year, feature presentations and Q&A sessions with study researchers and study team members.

[27] https://forteresearch.com/news/infographic/infographic-retention-in-clinical-trials-keeping-patients-on-protocols/
[28] https://www.ciscrp.org/download/2017-perceptions-insights-study-the-participation-experience/?wpdmdl=8770

Continued from page 39

– A PPMI Participant Webpage allows centralized access to digital versions of the participant newsletters and recordings of study update calls.

+ Express appreciation through a thank-you booklet: Letters from members of the Parkinson's community, researchers, MJFF staff, statisticians and study coordinators were published in a print and digital booklet to thank and honor volunteers for their participation. Collecting the personal reflections of the many individuals involved in or impacted

by PPMI is a meaningful way to empower participants and remind them of the larger cause they are tied to.

+ Inform participants of study results through newsletters, update calls and a webpage: The majority of study volunteers (90 percent) want to receive results from the clinical trial in which they participated. Because there is ongoing analysis of PPMI data and continued follow up of participants, study results are shared on a rolling basis. Using familiar channels to communicate study progress is a great way to close the loop with study participants.

Putting it All Together: Host an Event

PPMI staff and study leadership also show their commitment to the study's success, and their appreciation for participants, by hosting annual study update luncheons and dinners that incorporate all the tenets of retention. Having an in-person get together gives participants the chance to meet other volunteers and share experiences of living with PD and taking part in PPMI. During these events, local site staff present study progress and provide relevant results from ongoing data analysis. Foundation staff also attend and, together, all study stakeholders thank participants for their time and commitment.

[29] Getz, Kenneth. "Events That Have Shaped Study Participant Protection." *The Gift of Participation: a Guide to Making Informed Decisions about Volunteering for a Clinical Trial*, 2nd ed., CISCRP, Center for Information & Study On Clinical Research Participation, 2014, pp. 158–158

To facilitate the development and execution of a retention strategy, The Michael J. Fox Foundation has created a Recruitment and Retention Toolkit. The toolkit comprises of materials to: 1) facilitate participation; 2) communicate study progress; 3) express appreciation; and 4) share results. The toolkit contains customizable templates and how-to guides. Within the toolkit, certain materials are patient-facing (i.e., research teams will distribute them to individuals with PD and/or their care partners to facilitate participation), while others can be used with both participants and site staff to communicate about study progress, express appreciation and share results. For additional information, materials in the Recruitment and Retention Toolkit, and to start building your retention strategy, visit michaeljfox.org/ResourcePack.

The Michael J. Fox Foundation's Recruitment and Retention Toolkit

| Educate on Research Participation | Generate Study Awareness | Guide Through Consent | Facilitate Participation | Communicate Progress & Appreciate Participants | Share Study Results |

Learn more at
michaeljfox.org/ResourcePack

Chapter 4
Key Takeaways

+ Form a retention committee early in the planning process to understand participant and site staff goals, off-ramps and touchpoints to facilitate long-term engagement in the study.

+ Develop a retention strategy that focuses on facilitating participation, communicating study progress, expressing appreciation and sharing results. Focus this strategy on study participants and site staff.

+ Use MJFF's Recruitment and Retention Toolkit to make it easy to plan your retention strategy.

Glossary

As you read the manual "Accelerating Clinical Trials: Best Practices for Recruitment and Retention," please refer to this list for definitions of terms that may be unfamiliar.

DaTscans™

DaTscan is a specialized imaging technique that uses small amounts of a radioactive drug to evaluate the dopamine-producing cells in the brain. By itself, it cannot diagnose Parkinson's, but it can help confirm a doctor's diagnosis. DaTscan is being studied as a possible biomarker of Parkinson's.

Electronic Patient Reported Outcomes (ePROs)

Data that is provided directly by participants using electronic means such as smartwatches, sensors and monitors. These data complement traditional measures used during in-person clinical trial and study visits to give researchers a more complete picture of disease.

Hoehn and Yahr Scale

The Hoehn and Yahr (H&Y) scale divides PD into stages based on the severity of motor symptoms. Clinical trials often include H&Y stages as part of their eligibility criteria so that they can ensure that the intervention evaluated will include people with the right symptoms.

Institutional Review Board (IRB)

An independent committee of scientists, doctors and others (usually at least one "non-scientific" person who represents the patient voice) that evaluates and approves each study's protocol and informed consent document, and monitors ongoing study activities. The Institutional Review Board (IRB) is in place to protect the rights and welfare of people participating in a study.

Organic Marketing

A term in marketing that refers to the act of generating attention for and driving customers to a product or service without the use of any paid advertisements.

Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS)

The Unified Parkinson's Disease Rating Scale (UPDRS) was developed in the 1980s and has become the most widely used clinical rating scale for Parkinson's disease. A Movement Disorder Society (MDS) sponsored critique in 2001 expanded and revised the scale. The MDS-UPDRS scale is comprised of four key components: I: Non-motor Experiences of Daily Living; II: Motor Experiences of Daily Living; III: Motor Examination; and IV: Motor Complications.[1]

MDS-UPDRS PART II

Section II of the MDS-UPDRS evaluates the "Motor experiences of daily living." This includes activities such as eating, sleeping and writing. Section II is comprised of 13 questions and is self-administered by participants, with or without the aid of the caregiver but independently of the investigator.[2]

Modified Schwab & England Activities of Daily Living Scale

The Modified Schwab & England Activities of Daily Living scale assesses an individual's ability to function in activities of daily living. The scale ranges from zero to one hundred percent, with one hundred percent indicating a completely independent individual.[3] This assessment is typically conducted as part of a larger exam, such as the MDS-UPDRS.

The Montreal Cognitive Assessment (MoCA) Exam

The MoCA exam is a rapid screening instrument for mild cognitive dysfunction. It assesses attention, planning and memory skills. The total possible score is 30 points with a score of 26 or higher indicating no dysfunction.

Scales for Outcomes in Parkinson's Disease – Autonomic Dysfunction (SCOPA-AUT) Exam

The SCOPA-AUT exam assesses autonomic symptoms in patients with Parkinson's disease (PD). The questionnaire consists of 25 items assessing the following regions: gastrointestinal, urinary, cardiovascular, thermoregulatory, pupillomotor and sexual dysfunction.[4]

Steering Committee

Is a group of experts (such as clinical trial investigators, patient advisory groups and sponsor representatives) appointed by a study sponsor to provide overall supervision of a trial and ensure it is being conducted in accordance with the principles of Good Clinical Practice and the relevant regulations.[5]

University of Pennsylvania Smell Identification Test (UPSIT) Exam

The UPSIT exam assesses an individual's loss of smell. The test is comprised of forty microencapsulated odorants, which are released by scratching standardized odor-impregnated test booklets. The UPSIT is sensitive to age, gender, smoking habits, and a wide variety of olfactory disorders.[6]

[1] https://www.movementdisorders.org/MDS-Files1/PDFs/Rating-Scales/MDS-UPDRS_Vol23_Issue15_2008.pdf

[2] https://www.sralab.org/rehabilitation-measures/movement-disorder-society-sponsored-unified-parkinsons-disease-rating-0

[3] http://www.virtualhospice.ca/en_US/Main+Site+Navigation/Home/For+Professionals/For+Professionals/Tools+for+Practice/Assessment+tools/ Schwab+_+England+Activities+of+Daily+Living+Scale+(Parkinson_s+Disease).aspx

[4] https://www.ncbi.nlm.nih.gov/pubmed/15390007

[5] https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm127073.pdf

[6] http://theotorhinolaryngologist.co.uk/new/images/pdf/v6_n2/upsit.pdf

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