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Research Report

Use of an Online Portal to Facilitate Clinical Trial Recruitment: A Preliminary Analysis of Fox Trial Finder

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Abstract.
Background: As in other therapeutic areas, clinical studies in Parkinson's disease (PD) face significant recruitment challenges. However, qualitative surveys suggest that individuals with PD are willing to participate in clinical research. The Michael J. Fox Foundation therefore established Fox Trial Finder in 2011 to facilitate connection between PD research teams and volunteers.
Objective: Characterize the research volunteers (with and without PD) registered on Fox Trial Finder as of June 2014, and the published, recruiting studies to identify trends and highlight gaps between research requirements and available volunteers.
Methods: Profiles of volunteers with and without PD were analyzed to explore trends in geography, demographics, family history and, for those volunteers with PD, disease progression and treatment history. Clinical study profiles were analyzed to determine study type, phase, sponsor, focus, location and eligibility criteria. The analysis focused on volunteers and studies based in the United States.
Results: The database contained 26,261 US-based volunteers, including 19,243 volunteers (73%) with PD and 7,018 (27%) controls without PD. The average time since diagnosis for PD volunteers was 5.7 years and the average age at diagnosis was 58 years. Control volunteers were more likely than volunteers with PD to be female (67% vs. 35%) and to have a family history of PD (49% vs. 12%).
Conclusions: Fox Trial Finder's registration history to date demonstrates the high level of willingness among individuals affected by PD to participate in clinical research and provide a significant amount of personal health information to facilitate that participation.

Keywords: Parkinson's disease, patient recruitment, research subject recruitment, clinical trial, observational study

INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disease in the world, affecting an estimated five million individuals. Prevalence is forecasted to grow dramatically as the population ages [1]. Many advances in the disease etiology have been made over the past decade; however, new symptomatic and disease-modifying treatments are needed to improve the quality of life for patients [2].

Clinical study recruitment poses a challenge to research across therapeutic areas. According to one source, only one-third of studies conducted in the United States and Western Europe enroll patients consistently without recruitment challenges [3]. A 2013 study from the Tufts Center for the Study of Drug Development based on 150 clinical studies and 16,000 sites found that, while nine out of 10 clinical trials eventually meet their goals for patient enrollment, doing so typically requires doubling of the original trial timeline

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[4]. Of particular interest in PD, elderly populations do not commonly partake in clinical research due to such barriers as comorbidities, communication or cognitive challenges, transportation difficulties or low income [5]. Focus groups with the public and caregivers conducted by the NIH in 2011 showed that both groups were unfamiliar with, and therefore unwilling to participate in, clinical trials; however, after learning more about these opportunities, attitudes improved significantly [6].

The field of PD research faces additional unique scientific and recruitment challenges. Specifically, PD research is hampered by a lack of validated biomarkers, inappropriate animal models and limited understanding of this complex neurodegenerative disorder which affects multiple systems [7, 8]. Furthermore, a 2011 analysis of Medicare beneficiaries with PD in 2002 showed that only 58% of individuals with PD received neurologist care between 2002 and 2005 [9].

The challenges facing PD research and recruitment are not due to a lack of willing participants. Indeed, an informal survey of 832 individuals with PD conducted in 2012 by The Michael J. Fox Foundation for Parkinson's Research (MJFF) revealed that while 80% of respondents said they would be willing to participate in clinical studies, only 10% ever enrolled. Furthermore, we are in a particularly exciting time for PD research, with an increased understanding of PD and advances in genetics and with innovative therapeutic and biomarker studies underway [10–12]. As more promising therapies enter the clinic, the need for timely patient recruitment will only increase.

In an effort to accelerate PD clinical study recruitment for the field, MJFF created Fox Trial Finder (FTF), an online PD clinical studies matching tool. FTF aims to speed the flow of appropriate participants into the PD studies that urgently need them by: 1) assembling a database of willing volunteers searchable by key determinates of study eligibility; 2) collecting a comprehensive listing of actively recruiting PD clinical studies; and 3) providing a secure, anonymous one to one messaging platform by which interested participants and study team members can communicate directly.

Launched in the United States in July 2011, FTF has amassed a vast database of potential study participants and PD clinical studies. What follows is an analysis of registered Fox Trial Finder volunteers, including their location, demographics, disease progression, treatment regimens and family history. These results are compared to data on the types of PD studies being conducted, where they are actively recruiting, and the characteristics they are looking for in potential participants.

MATERIALS AND METHODS

FTF is a public facing website available at http://www.foxtrialfinder.org. It is currently available in English, French, Spanish, Italian and German and allows studies and volunteers to be registered globally. Explicit targeted outreach efforts are ongoing in the United States, Canada, the United Kingdom, Spain, France, Germany, Italy, Austria, Australia and Ireland.

Volunteer data collection

Volunteer data are collected when individuals interested in seeking out PD studies visit the website and follow the registration process, which allows them to submit their demographic and health information securely. The data points for PD volunteers, listed in Table 1, were identified by a review of the most common inclusion and exclusion criteria amongst PD clinical research conducted across industry and academia. Control volunteers submit demographic information, including age, gender and location, and any relevant family or genetic history of PD.

For all participants, the only required questions are: health status (volunteer with PD vs. control), zip code, and date of birth. All other questions are optional. Thus, in reporting results, the percentage of non-responding volunteers is noted.

Study data collection

All PD studies that have ethical approval to be conducted on human volunteers are eligible to recruit through FTF. Trials are posted to the website in one of two ways. First, they may be imported to FTF directly from http://www.clinicaltrials.gov via an import tool built into the website's code. Second, studies may be submitted directly to FTF by an investigator or other member of the study team. Trial profiles contain the following descriptive information: recruitment status, sites, title, summary of protocol, inclusion / exclusion criteria, study type / phase, sponsor type, principal investigator, study focus and whether the study is FDA regulated. In addition to the full inclusion / exclusion criteria, study profiles contain high-level information about patients who are eligible to participate in the study, including gender, age, time since diagnosis, Hoehn & Yahr (H&Y) stage, and whether any PD medications and / or surgical procedures either are

Table 1
Data points collected from FTF registrants (Data points included in the matching algorithm are noted with an asterisk)

Variable	Description
Name	
Email address	
How did you hear?	
PD status*	Described as "healthy control" or "diagnosed with PD"
Location / Second Location*	Determined by zip code, city, state, country
Distance willing to travel*	Range from 50–10,000 miles
Gender*	
Date of birth*	
Race/ethnicity	
Date diagnosed*	
Hoehn & Yahr*	Scale from 0–5 (no symptoms, symptoms 1 side, symptoms both sides, impaired balance but independent, severely disabled but able to walk or stand unassisted, wheelchair or bedridden)
Motor symptoms experienced	(Mark if yes) Resting tremor, falling/poor balance, trouble walking/shuffled gait, slowness, small handwriting
Non-motor symptoms experienced	(Mark if yes) Pain, memory loss, constipation, depression, lightheadedness/orthostatic hypotension, loss of smell, sleep disturbances)
Date symptoms began	Month/year
Medications currently taking*	(Mark if yes) Amantadine (Symmetrel), Apomorphine (Apokyn), Benztrophine (Cogentin), Bromocriptine (Parlodel), Carbidopa, levodopa and entacapone (Stalevo), Carbidopa-levodopa (Sinemet), Duodopa, Entacapone (Comtan), Levodopa-benserazide (Madopar), Melevodopa (Sirio), Pramipexole (Mirapex, Mirapex ER, Mirapexin, Sifrol), Rasagiline (Azilect), Ropinirole (Adartel, Requip, Requip XL, Ropark), Rotigotine (Neupro), Selegiline (l-deprenyl, Eldepryl, Zelapar), Tolcapone (Tasmar), Trihexyphenidyl (Apo-Trigex, Artane)
Medications taken in the past*	(Mark if yes) to same list as above
Medications never taken	(Mark if yes) to same list as above
Date medication began*	Month/year
Experiencing on/off fluctuations	(Mark if yes)
Experiencing compulsive behavior (gambling, spending, etc.)	(Mark if yes)
Had DBS*	(Mark if yes)
Had other neurosurgery*	(Mark if yes)
Supplements currently taking*	(Mark if yes) CoQ10, Creatine, Inosine, Vitamin C, Vitamin D, Vitamin E
Supplements taken in the past*	(Mark if yes) to same list above
Supplements never taken*	(Mark if yes) to same list as above
Family history of PD	(Mark if yes) Aunt, child, father, grandchild, grandparent, half sibling, mother, nephew, niece, sibling, uncle
Genetic testing	(Mark if yes) Haven't been tested/Was tested but do not know results
Confirmed genetic mutation	(Mark if yes) PARK1/PARK4/SNCA or alpha-synuclein, PARK2/PARKIN, PARK6/PINK1, PARK7/DJ-1, PARK8/LRRK2 or dardarin, no mutation
Participated in previous studies	(Mark if yes)
Actions taken as a result of FTF	(Mark if yes) Reviewed trial details for at least one trial, utilized the FTF messaging system or email to inquire about a trial, inquired about a trial over the phone, participated in an in-person visit to the trial site, enrolled in a clinical trial, other

mandatory for inclusion or would exclude a patient from being eligible to participate. Profiles also note whether the study is accepting control volunteers.

Matchmaking

Once a study is posted, registered study team member(s) receive a de-identified list of all potentially eligible volunteers based on the website's proprietary matching algorithm. Data points that factor into the matching algorithm are marked with an asterisk in Table 1.

Trial team members can send secure messages to the de-identified volunteers of interest using the FTF messaging system.

Once registered, a volunteer receives a list of the study "matches" that they may qualify for based on the information they provided in the registration process. Volunteers also have the ability to send secure messages to the study teams recruiting for the studies

in which they are interested. A high-level overview of this process is presented in Fig. 1.

The dataset

As of July 2014, the volunteer dataset contains 32,242 unique volunteer profiles, 71% of which represent individuals with PD. Each PD volunteer record contains up to 99 variables specific to that individual. The study data set contains 471 recruiting studies. Note that, throughout the manuscript, the term "study" is used to refer to both interventional clinical trials and observational clinical studies. Because FTF did not launch internationally until November 2013, not enough data exist to conduct a robust analysis nor can trends in these countries yet be identified. Thus, the current analysis is focused on FTF data from the US.

The following analysis pertains to the 26,261 volunteers and 329 studies registered with a location in the United States at the time of the analysis (July 2014).

RESULTS

Volunteers

As noted above, the dataset contains 32,242 unique volunteer profiles as of July 2014. Individuals with PD make up 71% of these volunteers; the remaining 29% are volunteers without Parkinson's disease who want to participate in Parkinson's research. As discussed above, the following analysis pertains to the subset of 26,261 volunteers registered with a location in the United States. Of these, 19,243 volunteers (73%) have Parkinson's disease, and 7,018 (27%) are controls.

The full set of questions that volunteers are asked to answer is provided in Table 1. All of the volunteer data provided in FTF is self-reported. In an effort to encourage as many volunteers as possible to register for the website, profile questions are not mandatory. Thus, for each of the characteristics listed below, we note the percentage of volunteers who provided a response.

Baseline characteristics (demographics, gender, age ethnicity, geography, family history) (Table 2)

Overall, volunteers with PD were more likely to be male (55% vs. 26% of respondents) and older (median age of 63 vs. 50 years) than volunteers without PD. Both populations reported white / Caucasian as their primary ethnicity (84.8% vs. 86.1%). Note that volunteers were allowed to report multiple ethnicities; therefore, the percentage of respondents reporting an ethnicity sums to more than 100%.

Volunteers' geographic data was grouped by core based statistical area (CBSA). CBSAs are defined geographic entities used by the Federal Office of Management and Budget to publish population data. "Metro" CBSAs contain a core urban area of 50,000 or more inhabitants, while "micro" CBSAs contain an urban core of at least 10,000 inhabitants [13]. The most common CBSA reported by both groups of volunteers was New York-Northern New Jersey. The Los Angeles, Chicago, Phoenix, Atlanta and Houston areas were all other top CBSAs reported by both groups.

Only a small percentage of the 19,243 PD volunteers (2,298, or 12%) reported a history of Parkinson's disease in their immediate family. Family history was most commonly reported in the father (728 respondents, or 3.8%). In contrast, a family history of PD was reported by 3,411 of 7,018 control volunteers (48.6%), with more than half of those respondents (54.1%) listing their father as having a diagnosis of PD. The higher rates of family history reported by control volunteers may be driven by a family connection to PD fostering interest in research participation.

PD volunteers: Clinical features (Table 3)

Time since diagnosis: The average time since diagnosis for PD volunteers was 5.7 years (median: 6.0 years). The average age at diagnosis was 58 years (this was also the median age at diagnosis). 909 patients (4.7% of 19,243) reported having young-onset Parkinson's. The average age of these patients was 43 years, and their average age at diagnosis was 33 years.

H&Y status: Volunteers' self-reported H&Y status is listed below in Table 3. FTF does not ask patients directly for their H&Y status, since they are unlikely to be familiar with this terminology; rather, they are asked to qualitatively describe the extent of their PD symptoms using the language shown in Table 3. Over one-third (35.6%) of PD volunteers reported experiencing PD symptoms on only one side of the body (H&Y Stage 1); these patients were eligible for 83% of the recruiting studies on FTF.

Motor & non-motor symptoms: The most commonly reported symptom was slowness of movement, with nearly 58% of individuals with PD saying they experienced this symptom. Resting tremor was the only other symptom reported by more than 50% of patients, with 55.6% reporting it. Interestingly, although motor symptoms are considered to be the hallmark presentation of Parkinson's disease, sleep disturbance – a

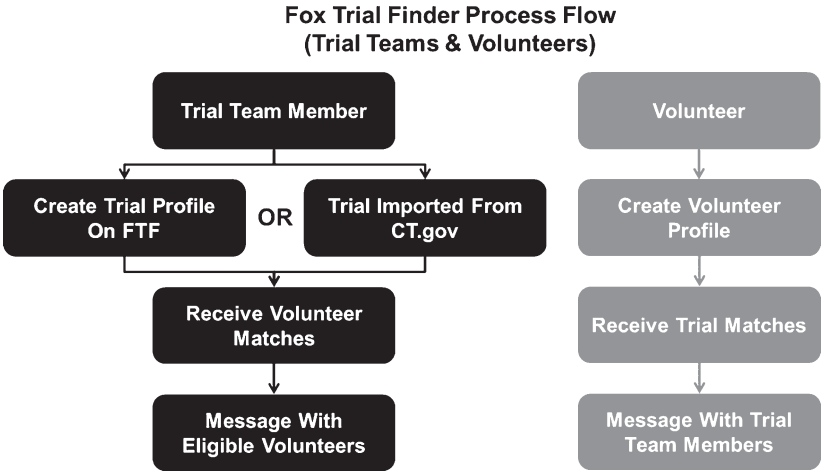

Fig. 1. FTF process flow.

non-motor symptom – was the third-most common symptom, reported by 48.8% of PD volunteers. For a full list of symptoms, see Table 3.

Procedure history: A history of PD-related neurosurgery was relatively rare among volunteers with PD. Nine hundred forty-nine PD volunteers (4.9% of the sample) reported a history of deep brain stimulation, while 173 volunteers (0.9%) reported a history of another form of neurosurgery.

Medication history: The most commonly reported medication that volunteers reported using was Sinemet (carbidopa-levodopa), with over 50% of volunteers taking it at the time of analysis or having taken it in the past. The next most common medication was Azilect (rasagiline), with 28.7% of patients reporting current or past use. Current or past use of Mirapex (pramiprexole) was reported by 26.9% of patients. For a full list of medications taken by PD volunteers, see Table 4. Table 4b contains the same information but breaks the data out by volunteers' self-reported H&Y status.

Trials

As of July 2014, there were 329 studies recruiting across the United States on FTF. Because many studies recruit at multiple clinical sites, the 329 studies were recruiting at a total of 627 sites. While each "site" was a unique location for a given study, one site (e.g. a university medical center) may recruit for multiple studies simultaneously. Thus, it should not be assumed that there were 627 unique facilities or institutions recruiting.

Sponsor type: Of the 329 recruiting studies, 130 (40%) were sponsored by an academic institution, 50 (15%) by the National Institutes of Health, 69 (21%) by industry, 32 (10%) by foundations or other Parkinson's-focused organizations, 16 (5%) by the Federal Government (outside of the NIH) and 12 (4%) by a hospital or other medical center. 20 studies did not specify a sponsor type.

Geography: Three CBSAs had the greatest prevalence of recruiting PD clinical research. There were 31 sites recruiting in the immediate New York City area, 30 in the Washington, DC area and 28 in the Chicago area. The Boston, MA and Portland, OR areas each had 21 sites recruiting for PD research. For a full list of sites recruiting by geography, see Table 5.

Study type and phase: Fifty-one percent of recruiting studies were considered interventional, while 49% were observational. Of the interventional trials, 18% were Phase I, 22% Phase II, 15% Phase III and 7% Phase IV. Sixty-four interventional trials did not specify a phase.

Study focus: When a study posting is created on FTF, the person creating the posting can specify the area of focus to describe the key area(s) being researched in the study. FTF allows researchers to specify any of 23 areas of focus that represent common themes in PD research. Those areas are: anxiety, apathy, biomarkers, bradykinesia / rigidity, cause of PD, cognitive deficits, constipation / bladder problems, depression, dyskinesia, dysphagia, fatigue, gait disturbances (e.g. freezing), genetics, hypotension, impulse control, neuroprotection, pain, postural instability (e.g. falling), sexual dysfunction, sialorrhea, sleep disturbances, speech difficulties and tremors. Researchers can select as many focus areas as are relevant to their study, though selection is not mandatory.

Table 2
Demographic characteristics of the FTF population

Attribute	Individuals with PD (n = 19,243)	Controls (n = 7,018)
Age		
Mean (Years)	62	51
Median (Years)	63	50
No Response (# of respondents, %)	560 (3%)	170 (2%)
Gender (# of respondents, %)		
Male	10,489 (55%)	1,647 (26%)
Female	6,735 (35%)	4,706 (67%)
No Response	2,019 (10%)	665 (9%)
Ethnicity (# of respondents, %)[a]		
No Response	1,635 (8.5%)	534 (7.6%)
White or Caucasian	16,314 (84.8%)	6,039 (86.1%)
Hispanic or Latino	620 (3.2%)	287 (4.1%)
Asian	416 (2.2%)	168 (2.4%)
American Indian or Alaska Native	287 (1.5%)	121 (1.7%)
Black or African American	272 (1.4%)	81 (1.2%)
Native Hawaiian or Pacific Islander	64 (0.3%)	20 (0.3%)
Location (# of respondents, %)[b]		
New York-Northern New Jersey NY-NJ[c,d]	562 (2.9%)	416 (5.9%)
Los Angeles-Western Suburbs, CA[c,d]	466 (2.4%)	160 (2.3%)
Chicago Northern Suburbs, IL-WI[c,d]	456 (2.4%)	249 (3.5%)
Phoenix-Mesa-Glendale, AZ[c,d]	330 (1.7%)	118 (1.7%)
Atlanta-Sandy Springs-Marietta, GA[c,d]	301 (1.6%)	141 (2.0%)
Houston-Sugar Land-Baytown, TX [c,d]	291 (1.5%)	108 (1.5%)
Fairfax Co., VA±	273 (1.4%)	155 (2.2%)
San Diego-Carlsbad-San Marcos, CA[c,d]	267 (1.4%)	92 (1.3%)
Philadelphia Western Suburbs, PAc	265 (1.4%)	149 (2.1%)
Dallas North Suburbs, TX[d]	262 (1.4%)	88 (1.3%)
Denver-Aurora-Broomfield, CO[c,d]	254 (1.3%)	79 (1.1%)
Minneapolis-St. Paul-Bloomington, MN-WI±	243 (1.3%)	107 (1.5%)
Seattle Southern Suburbs, WA[c,d]	236 (1.2%)	112 (1.6%)
Los Angeles SE Suburbs, CA	234 (1.2%)	56 (0.8%)
Sacramento-Arden-Arcade-Roseville, CA	230 (1.2%)	70 (1.0%)
San Francisco Eastern Suburbs, CA[d]	222 (1.2%)	101 (1.4%)
Riverside-San Bernardino-Ontario, CA	221 (1.1%)	48 (0.7%)
San Francisco Peninsula Suburbs, CA[d]	203 (1.1%)	113 (1.6%)
New York-Long Island, NY[d]	202 (1.0%)	92 (1.3%)
Northern Jersey Suburbs, NJ	193 (1.0%)	58 (0.8%)
Family History of PD (# of respondents, %)		
Father	1,008 (5.2%)	1,845 (54.1%)
Mother	728 (3.8%)	1,148 (33.7%)
Sibling	537 (2.8%)	355 (10.4%)
Child	25 (0.1%)	63 (1.8%)

a: Respondents are allowed to select multiple ethnicities; thus, percentages will not add to 100%. b: Note that this list includes only the top 20 core-based statistical areas (CBSAs) for volunteers with PD, representing 29.7% of the total sample of 19,243 volunteers with PD. Overall, there were 823 CBSAs reported by 19,243 volunteers with PD and 582 CBSAs reported for 7,018 controls. c: Indicates a CBSA that was in the top 20 for both study sites and PD volunteers. d: Indicates a CBSA that was in the top 20 for both PD and control volunteers.

Of the 329 studies listed on FTF at the time of the analysis, nearly half (159 studies, 48%) of all PD clinical studies recruiting on FTF reported a key focus area of motor symptoms of PD (gait disturbances: 39 studies, postural instability: 29 studies, bradykinesia: 49 studies, tremors: 42 studies). Biomarkers (16%,

Table 3
Clinical features of FTF volunteers with PD

Attribute	# of respondents (%)
H&Y Status	
No Response	2,970 (15.4%)
0: No PD symptoms or complaints	4,030 (20.9%)
1: Experiencing PD symptoms on one side of the body	6,849 (35.6%)
2: Experiencing PD symptoms on both sides of the body	3,835 (19.9%)
3: Impaired balance, but still independent	291 (1.5%)
4: Severely disabled, but able to walk or stand unassisted	884 (4.6%)
5: Wheelchair or bedridden unless assisted	384 (2.0%)
Motor Symptoms[a]	
Falling, Poor Balance	5,696 (29.6%)
Resting Tremor	10,698 (55.6%)
Slowness	11,147 (57.9%)
Micrographia (Small Handwriting)	9,246 (48.0%)
Trouble Walking / Shuffled Gait	8,392 (43.6%)
Non-Motor Symptoms[a]	
Constipation	6,726 (35.0%)
Depression	6,074 (31.6%)
Orthostatic Hypotension / Lightheadedness	4,118 (21.4%)
Hyposmia (Loss Of Smell)	6,646 (34.5%)
Memory Loss	5,425 (28.2%)
Pain	5,896 (30.6%)
Sleep Disturbance	9,397 (48.8%)
Procedure History (# of respondents, %)	
Deep Brain Stimulation	949 (4.9%)
Other Neurosurgery	173 (0.9%)

a: Volunteers check a box to confirm they experience specific symptoms. An unchecked box can mean that a volunteer does not experience that symptom, or simply that a volunteer did not answer the question.

52 studies), cognitive deficits (15%, 50 studies) and depression /anxiety (10%, 32 studies) were other frequently reported areas of focus.

Eligibility criteria (Age, time since diagnosis and disease progression): Forty percent of studies accepted controls and 100% accepted individuals with PD. The median minimum age for inclusion was 21; the median maximum age was 95. Time since PD diagnosis did not appear to be a major factor in the determination of study eligibility. Only 25 studies (8%) specified a minimum time since diagnosis and only 37 (11%) specified a maximum time since diagnosis. Of those that specified a minimum time since diagnosis, the mean was 2.8 years (range: 0–5 years). Of those that specified a maximum time since diagnosis, the mean was 22.9 years (range: 0–60 years).

Individuals with PD with an H&Y score of 2 were eligible for 85% of the 329 recruiting studies. This is more than any other stage of disease progression, including those who were at a stage of zero (74%) or one (83%). Patients with an H&Y score of 5 were eligible for the smallest percentage of studies (66%).

Eligibility criteria (Treatment and surgical history): 62 studies (19%) took either past or current medication use into account when determining a patient's eligibility. Of these 62 studies, it was more common to *disqualify* a patient based on current or past medication use, rather than to *require* a patient be taking or have taken a specific medication in the past. The most common drug to disqualify a patient from a study was selegiline. There are 25 studies that disqualified patients who are taking Comtan, and 12 that disqualified patients who have taken Comtan in the past. Stalevo (carbidopa / levodopa / entacapone) was the most commonly required drug; 19 studies required that a patient be taking Stalevo. A full list of inclusion and exclusion criteria by medication history is listed in Table 6.

Regarding surgical history, patients with DBS were eligible for 73% of studies, and those who have had another neurosurgery were eligible for 81%.

DISCUSSION

FTF was established with the goal of bringing PD researchers together with a large pool of willing, eligible volunteers. The consistent growth in volunteer registrations over time, with over 32,000 volunteers in the first three years, demonstrates the continued interest of the PD community to participate in research. This enthusiasm is particularly notable in individuals with PD, who tend to be older (with a median age at diagnosis of 60).

One way that the utility of the site to both volunteers and study teams can be demonstrated is through messaging. As mentioned in the introduction, both volunteers and researchers can contact each other through Fox Trial Finder's secure messaging system. (All volunteers are de-identified in this process to protect confidentiality. Additionally, only researchers who are connected to actively recruiting IRB-approved studies can message volunteers.) Since the messaging system went live in July 2011, researchers have initiated over 43,200 messages with volunteers to screen them for studies. Volunteers, in turn, have initiated over 11,600 messages with researchers. While these numbers underscore the compelling nature of FTF, they do not capture any solicitations that take place outside of FTF (i.e. over email or telephone for researchers whose

Table 4
Self-reported medication history of volunteers with PD

	Currently taking	Taken in past	Never taken	No response
Amantadine	2,069 (10.8%)	1,445 (7.5%)	6,485 (33.7%)	9,244 (48%)
Apomorphine	58 (0.3%)	140 (0.7%)	8,536 (44.4%)	10,509 (54.6%)
Benztropine	105 (0.5%)	249 (1.3%)	8,378 (43.5%)	10,511 (54.6%)
Bromocriptine	22 (0.1%)	118 (0.6%)	8,399 (44%)	10,704 (56%)
Carbidopa, levodopa and entacapone	1,996 (10.4%)	1,087 (5.6%)	7,181 (37.3%)	8,979 (46.7%)
Carbidopa-levodopa	8,702 (45.2%)	1,210 (6.3%)	2,954 (15.4%)	6,377 (33.1%)
Duodopa	1 (0.01%)	7 (0.04%)	1,200 (6.2%)	18,035 (93.7%)
Entacapone	833 (4.3%)	892 (4.6%)	7,336 (38.1%)	10,182 (52.9%)
Levodopa-benserazide	215 (1.1%)	146 (0.8%)	8,295 (43.1%)	10,587 (55.0%)
Melevodopa	7 (0.04%)	12 (0.1%)	2,665 (13.8%)	16,559 (86.1%)
Pramiprexole	2,860 (14.9%)	2,310 (12.0%)	5,418 (28.2%)	8,655 (45.0%)
Rasagiline	3,786 (19.7%)	1,734 (9.0%)	5,247 (27.3%)	8,476 (44.0%)
Ropinirole	2,620 (13.6%)	2,220 (11.5%)	5,530 (28.7%)	8,873 (46.1%)
Rotigotine	285 (1.5%)	287 (1.5%)	2,348 (12.2%)	16,323 (84.8%)
Selegiline	723 (3.8%)	1,095 (5.7%)	7,258 (37.7%)	10,167 (52.8%)
Tolcapone	62 (0.3%)	141 (0.7%)	8,318 (43.2%)	10,722 (55.7%)
Trihexyphenidyl	427 (2.2%)	460 (2.4%)	7,777 (40.4%)	10,579 (55.0%)

study profiles list this information). Thus, volunteers likely are reaching out to researchers at a higher rate than can be captured via FTF. As more pipeline agents for PD move into clinical-stage testing, it will be interesting to see if messaging activity on FTF increases with the growth in clinical trial participation opportunities.

Our analysis identified some interesting trends with regard to the geographic overlap between study sites and volunteers. Only 5 of the top 10, and 10 of the top 20, CBSAs for study sites were also in the top 20 sites for PD volunteers. Indeed, some major areas for medical research in the United States – Portland, OR; Cleveland, OH; Boston, MA; Birmingham, AL – did not appear in the top 20 CBSAs for PD volunteers. This discrepancy between the location of willing volunteers and the studies that need them underscores the importance of a tool like FTF to facilitate access to volunteers who are in these areas.

We also discovered demographic differences between PD and control volunteers. Sixty-one percent of our PD volunteers were male with an average age of 64 and a median age of 65. In contrast, 26% of control volunteers are male, with an average age of 51 and a median age of 50. In addition, control volunteers were more likely than PD volunteers to report having a first-degree relative with PD. For example, whereas 42.6% of control volunteers reported having a parent with PD, only 9% of individuals with PD reported the same. This high rate of family history could have ramifications for the appropriateness of this population for participation in research, as some studies that recruit controls specifically exclude volunteers who have a family history of PD.

Limitations

The FTF database faces several limitations. First, an online platform by its nature requires the cognitive skills and dexterity to operate a computer, both of which may be challenging for later-stage patients with PD. Indeed, 76% of FTF volunteers with PD reported that their disease was in H&Y stages 0–2. Caregivers or other friends / family members can create a profile on behalf of a volunteer with PD who is unable to use the site him/herself, and MJFF is aware of several caregivers who have done exactly that.

All volunteer information is self-reported, and we cannot assess the rate of false positives or false negatives in patients' reporting. However, a recent study conducted by the University of Rochester used telemedicine visits to demonstrate a 97% agreement between self-reported PD diagnoses on FTF and the diagnosis that was verified by movement disorder specialists during virtual visits; these results provide some confidence that PD diagnoses as reported on FTF align with reporting from a Movement Disorder specialist [14].

A further limitation of self-reported volunteer data is its accuracy over time. PD is by nature a progressive condition, meaning that volunteer's symptoms, medication and surgical history will evolve from the time

Table 4b
Self-reported medication history of volunteers with PD by H&Y status (1 of 2)

	H&Y 0 ($n = 291$)				H&Y 1 ($n = 6,849$)				H&Y 2 ($n = 4,030$)			
	Currently taking	Taken in past	Never taken	No response	Currently taking	Taken in past	Never taken	No response	Currently taking	Taken in past	Never taken	No response
Amantadine	17 (6%)	5 (2%)	134 (46%)	135 (46%)	690 (10%)	447 (7%)	2,958 (43%)	2,754 (40%)	623 (15%)	383 (10%)	1,580 (39%)	1,444 (36%)
Apomorphine	1 (<1%)	2 (1%)	141 (48%)	147 (51%)	7 (<1%)	15 (<1%)	3,632 (53%)	3,195 (47%)	15 (<1%)	46 (1%)	2,166 (54%)	1,910 (54%)
Benztropine	0 (0%)	2 (1%)	139 (48%)	150 (52%)	34 (<1%)	65 (1%)	3,564 (52%)	3,186 (47%)	32 (1%)	63 (2%)	2,137 (52%)	1,798 (45%)
Bromocriptine	2 (1%)	4 (1%)	138 (47%)	147 (51%)	7 (<1%)	18 (<1%)	3,562 (52%)	3,262 (48%)	5 (<1%)	21 (1%)	2,148 (53%)	1,856 (46%)
Carbidopa, levodopa, entacapone	23 (8%)	9 (3%)	127 (44%)	132 (45%)	598 (9%)	233 (3%)	3,320 (48%)	2,698 (39%)	493 (12%)	314 (8%)	1,777 (44%)	1,446 (36%)
Carbidopa-levodopa	110 (38%)	11 (4%)	86 (30%)	84 (29%)	3,024 (44%)	459 (7%)	1,683 (25%)	1,683 (25%)	2,277 (57%)	295 (7%)	672 (17%)	786 (20%)
Duodopa	0 (0%)	0 (0%)	23 (8%)	268 (92%)	1 (<1%)	1 (<1%)	532 (8%)	6,315 (92%)	0 (0%)	1 (<1%)	291 (7%)	3,738 (93%)
Entacapone	3 (1%)	6 (2%)	136 (47%)	146 (50%)	190 (3%)	154 (2%)	3,366 (49%)	3,139 (46%)	239 (6%)	250 (6%)	1,837 (46%)	1,704 (42%)
Levodopa-benserazide	5 (2%)	3 (1%)	137 (47%)	146 (50%)	61 (1%)	36 (1%)	3,541 (52%)	3,211 (47%)	41 (1%)	33 (1%)	2,112 (52%)	1,844 (46%)
Melevodopa	0 (0%)	0 (0%)	49 (17%)	242 (83%)	3 (<1%)	5 (<1%)	1,154 (17%)	5,687 (83%)	0 (0%)	2 (<1%)	652 (16%)	3,376 (84%)
Pramiprexole	37 (13%)	12 (4%)	112 (38%)	130 (45%)	1,212 (18%)	705 (10%)	2,522 (37%)	2,410 (35%)	726 (18%)	646 (16%)	1,331 (33%)	1,327 (33%)
Rasagiline	55 (19%)	14 (5%)	108 (37%)	114 (39%)	1,982 (29%)	573 (8%)	2,182 (32%)	2,112 (31%)	929 (23%)	489 (12%)	1,282 (32%)	1,330 (33%)
Ropinirole	23 (8%)	11 (4%)	120 (41%)	137 (47%)	1,031 (15%)	708 (10%)	1,578 (38%)	2,532 (37%)	666 (17%)	634 (16%)	1,347 (33%)	1,383 (34%)
Rotigotine	3 (1%)	2 (1%)	44 (15%)	242 (83%)	103 (2%)	97 (1%)	1,042 (15%)	5,607 (82%)	91 (2%)	82 (2%)	553 (14%)	3,304 (82%)
Selegiline	12 (4%)	6 (2%)	127 (44%)	146 (50%)	297 (4%)	222 (3%)	3,259 (48%)	3,071 (45%)	201 (5%)	319 (8%)	1,808 (45%)	1,702 (42%)
Tolcapone	0 (0%)	2 (1%)	141 (48%)	148 (51%)	12 (<1%)	19 (<1%)	3,539 (52%)	3,279 (48%)	18 (<1%)	31 (1%)	2,123 (53%)	1,858 (46%)
Trihexyphenidyl	1 (<1%)	1 (<1%)	137 (47%)	152 (52%)	217 (3%)	138 (2%)	3,307 (48%)	3,187 (47%)	112 (3%)	140 (3%)	1,976 (49%)	1,802 (45%)

Table 4b
Self-reported medication history of volunteers with PD by H&Y status (2 of 2)

	H&Y 3 ($n = 3,835$)				H&Y 4 ($n = 884$)				H&Y 5 ($n = 334$)			
	Currently taking	Taken in past	Never taken	No response	Currently taking	Taken in past	Never taken	No response	Currently taking	Taken in past	Never taken	No response
Amantadine	563 (15%)	424 (11%)	1,316 (34%)	1,532 (40%)	100 (11%)	110 (12%)	283 (32%)	391 (44%)	32 (8%)	51 (13%)	129 (34%)	172 (45%)
Apomorphine	27 (1%)	51 (1%)	1,910 (50%)	1,847 (48%)	6 (1%)	18 (2%)	399 (45%)	461 (52%)	2 (1%)	8 (2%)	164 (43%)	210 (55%)
Benztropine	25 (1%)	80 (2%)	1,867 (49%)	1,863 (49%)	8 (1%)	26 (3%)	392 (44%)	458 (52%)	3 (1%)	10 (3%)	161 (42%)	210 (55%)
Bromocriptine	5 (<1%)	46 (1%)	1,883 (49%)	1,901 (50%)	3 (<1%)	21 (2%)	391 (44%)	469 (53%)	0 (0%)	7 (2%)	160 (42%)	217 (57%)
Carbidopa, levodopa, entacapone	624 (16%)	359 (9%)	1,440 (38%)	1,412 (37%)	166 (19%)	103 (12%)	283 (32%)	332 (38%)	62 (16%)	48 (13%)	122 (32%)	152 (40%)
Carbidopa-levodopa	2,353 (61%)	309 (8%)	400 (10%)	773 (20%)	556 (63%)	81 (9%)	48 (5%)	199 (23%)	224 (58%)	34 (9%)	25 (7%)	101 (26%)
Duodopa	0 (0%)	3 (<1%)	255 (7%)	3,577 (93%)	0 (0%)	2 (<1%)	58 (7%)	824 (93%)	0 (0%)	0 (0%)	23 (6%)	361 (94%)
Entacapone	293 (8%)	323 (8%)	1,489 (39%)	1,730 (45%)	72 (8%)	95 (11%)	285 (32%)	432 (49%)	18 (5%)	48 (13%)	125 (33%)	193 (50%)
Levodopa-benserazide	78 (2%)	38 (1%)	1,851 (48%)	1,868 (49%)	22 (2%)	22 (2%)	379 (43%)	461 (52%)	8 (2%)	11 (3%)	156 (41%)	209 (54%)
Melevodopa	3 (<1%)	5 (<1%)	592 (15%)	3,235 (84%)	0 (0%)	0 (0%)	123 (14%)	761 (86%)	1 (<1%)	0 (0%)	51 (13%)	332 (86%)
Pramiprexole	671 (17%)	670 (17%)	1,067 (28%)	1,427 (37%)	118 (13%)	172 (19%)	217 (25%)	377 (43%)	46 (12%)	74 (19%)	96 (25%)	168 (44%)
Rasagiline	654 (17%)	479 (12%)	1,196 (31%)	1,506 (39%)	92 (10%)	104 (12%)	279 (32%)	409 (46%)	26 (7%)	50 (13%)	120 (31%)	188 (49%)
Ropinirole	662 (17%)	632 (16%)	1,070 (28%)	1,471 (38%)	148 (17%)	131 (15%)	236 (27%)	369 (42%)	44 (11%)	68 (18%)	102 (27%)	170 (44%)
Rotigotine	64 (2%)	84 (2%)	513 (13%)	3,174 (83%)	9 (1%)	16 (2%)	112 (13%)	747 (85%)	10 (3%)	6 (2%)	42 (11%)	326 (85%)
Selegiline	171 (4%)	383 (10%)	1,506 (39%)	1,775 (46%)	29 (3%)	102 (12%)	319 (36%)	434 (49%)	5 (1%)	39 (10%)	140 (36%)	200 (52%)
Tolcapone	19 (<1%)	53 (1%)	1,860 (49%)	1,903 (50%)	9 (1%)	23 (3%)	375 (42%)	477 (54%)	4 (1%)	12 (3%)	161 (42%)	207 (54%)
Trihexyphenidyl	68 (2%)	125 (3%)	1,727 (45%)	1,915 (50%)	18 (2%)	35 (4%)	364 (41%)	467 (53%)	6 (2%)	9 (2%)	162 (42%)	207 (54%)

they first create their FTF profile. While MJFF attempts to maintain a high level of engagement with volunteers and actively encourages them to update their profiles regularly, we cannot control how frequently volunteers take this step.

Additionally, only a small subset of volunteer questions (PD status, zip code and date of birth) is mandatory and many questions do not allow a patient to respond in the negative. For example, patients can indicate whether they have a history of deep brain stimulation or other neurosurgery, but there is no option to state that they have no surgical history. As a result, we cannot interpret a lack of response for an individual patient. Lastly, we must acknowledge the potential for selection bias in the patients who choose to register for FTF; therefore, these results cannot be generalized to the broader PD population.

Regarding study data, all information is either supplied by researchers who create study profiles or directly imported from clinicaltrials.gov. While FTF automatically imports updates to postings linked to clinicaltrials.gov, these postings often are not updated on a regular basis. For researcher-submitted studies, the site is dependent on researchers to maintain up-to-date profiles, which can create the same challenge.

Table 5
Study sites by CBSA

1.	New York-Northern New Jersey NY-NJ*	31
2.	Washington NE Suburbs, DC-MD	30
3.	Chicago Northern Suburbs, IL-WI*	28
4.	Boston Suburbs, MA	21
5.	Portland-Vancouver-Hillsboro, OR-WA	21
6.	Los Angeles-Western Suburbs, CA*	19
7.	Denver-Aurora-Broomfield, CO*	16
8.	Phoenix-Mesa-Glendale, AZ*	16
9.	New York-Long Island, NY	14
10.	Cleveland-Elyria-Mentor, OH	13
11.	Philadelphia Western Suburbs, PA*	13
12.	Birmingham-Hoover, AL	13
13.	Seattle Southern Suburbs, WA*	13
14.	San Jose-Sunnyvale-Santa Clara, CA	12
15.	Houston-Sugar Land-Baytown, TX*	11
16.	Baltimore-Towson, MD	11
17.	Atlanta-Sandy Springs-Marietta, GA*	10
18.	San Diego-Carlsbad-San Marcos, CA*	9
19.	Gainesville, FL	9
20.	Tampa-St. Petersburg-Clearwater, FL	9

*Indicates a CBSA that was in the top 20 for both study sites and PD volunteers.

Future directions

There are several potential future applications of the FTF model. First, while MJFF remains focused on PD, this model of compiling an eligible and willing volunteer population could be applied to other diseases and conditions. The Alzheimer's Prevention Registry and the Collaborative Clinical Research Network in Friedreich's Ataxia both represent other successful efforts to galvanize an eager volunteer population to support research [15, 16].

Second, opportunities exist to improve on FTF as it exists for PD research. For example, the variables that go into the matching algorithm are standardized across studies. Allowing researchers to tailor the algorithm to their study's eligibility criteria could generate higher-quality matches for both researchers and volunteers and could reduce the amount of time needed

Table 6
Number of trials that require or disqualify patients based on PD medication history

	Current		Past	
	Required	Disqualifies	Required	Disqualifies
Carbidopa / levodopa / entacapone	19	25	8	16
Bromicriptine	14	21	8	13
Ropinirole	15	23	8	14
Entacapone	13	19	7	10
Tolcapone	14	19	7	11
Rasagiline	13	23	7	11
Selegiline	13	25	7	12
Amantadine	15	22	7	12
Benztropine	14	24	7	13
Trihexyphenidyl	41	23	7	13
Pramipexole	14	22	8	14
Carbidopa-levodopa	17	24	8	14
Apomorphine	15	24	8	15
Levodopa-benserazide	16	22	8	13
Mevlevodopa	1	3	1	1
Rotigotine	1	3	1	1
Duopdopa	0	2	0	1

for screening after a patient is identified through FTF. Additionally, up to this point, FTF has been promoted predominantly to the patient and caregiver communities; more engagement with the physician and researcher communities could lead to increased use of the site by these important audiences.

Third, the willingness of these volunteers to participate in research could have implications for the types of studies that can be designed for the PD population. Only 10 of the top 20 CBSAs for PD volunteers were also in the top 20 study sites. Thus, there is a large sample of willing PD volunteers who do not have easy access to participate in a study that requires in-person participation. These volunteers have already demonstrated their comfort with online platforms by registering for FTF; studies that are conducted remotely (e.g. online, through telemedicine, etc.) could give volunteers an opportunity to participate in research while simultaneously giving researchers access to a volunteer population outside of their immediate region [17]. Many companies and academic institutions – including the University of Rochester, The Media Lab at the Massachusetts Institute of Technology, 23 and Me and others – are already conducting this type of research in PD, and more such studies are likely to arise as technology plays an increasing role in clinical research [18–20].

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CONFLICTS OF INTEREST

Ms. Rocker, Ms. Cappelletti, Ms. Marshall, Ms. Meunier, Ms. Brooks, Dr. Sherer and Ms. Chowdhury are all employees of The Michael J. Fox Foundation.

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