VERSION 2.0

PROTOCOL

Study Title:	Preferences and Perspectives on Early Intervention Trials
Sponsor:	The Michael J. Fox Foundation for Parkinson's Research (MJFF)
Principal Investigator:	Roseanne D. Dobkin, PhD
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EARLY INTERVENTION INTEREST SURVEY

PROTOCOL APPROVAL

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1. Purpose of the Study

The Parkinson's Progression Markers Initiative (PPMI) is a broad program consisting of the primary in-clinic study (PPMI Clinical), as well as other complementary initiatives conducted under the program that will contribute to PPMI's overarching goal to identify markers of disease progression for use in clinical trials of therapies to reduce progression of PD disability. PPMI study participants include people with manifest PD, prodromal PD, and healthy control volunteers.

Early intervention trials are currently being planned by scientific community. The overarching objective of this companion study (Early Intervention Interest Survey) is to better understand the preferences and perspectives of current PPMI prodromal participants regarding early intervention clinical drug trials for Parkinson's disease (PD).

This protocol is a web-based study conducted through the myPPMI portal. The online survey aims to evaluate the following areas: 1) general interest in early intervention clinical trials; 2) motivations for participation; 3) barriers to enrollment; 4) views on the risk-benefit balance of early intervention trials; and 5) perceptions of logistical factors (e.g., random assignment, travel, drug delivery) associated with study participation. Data will be utilized to support the further refinement of early intervention study design and methods, including the creation of recruitment materials and strategy, and the development of educational resources to support the participant journey, from the first point of contact with the study.

2. Background

Challenges to participant recruitment in clinical trials are well-known across all areas of research. Not surprisingly, it has been frequently documented that under-recruitment for clinical trials slows down medical research progress and increases expenses.[1] Approximately one-half (40% - 60%) of clinical studies fail to meet enrollment targets,[1] and low accrual rates are the most common single reason trials are prematurely terminated.[2]

Some common and significant barriers to clinical trial recruitment include competition for eligible study participants, burden on clinical trial sites, and burden on participants, among others.[1-3] Today, there are more than three times as many studies posted on clinicaltrials.gov as there were 10 years ago (157,913 in 2013; 477,237 in 2023; ClinicalTrials.gov data as of Feb 2, 2024). As scientific breakthroughs allow earlier detection of pathology[4], a growing number of new studies are exploring etiology as well as novel interventions focused on disease modification and prevention.

Recruiting individuals at the earliest stage of disease, often before people can self-identify their condition or receive a formal clinical diagnosis, poses additional challenges. Traditional research recruitment methods are inadequate for such populations since these individuals do not present to medical care or clinical trial opportunities related to the condition under study. Furthermore, such individuals may not recognize their own personal risk of the particular condition, and hence not self-refer for studies of this nature. Additionally, it is important — perhaps more so in an undiagnosed population — to communicate with potential participants in a way that provides needed education and can address concerns that may otherwise interfere with participation.

Early intervention trials are currently being planned by the scientific community. PPMI participants with biological risk factors for the development of PD and very early clinical symptoms of PD may be eligible to participate. Early intervention trials will test treatments to slow or stop disease. The conduct of clinical

trials in early disease populations is a new area of research; there is much to learn about how to best conduct studies in these patient groups.

To support the design and launch of future early intervention trials for PD, this web-based survey study will examine participant interest as well as various personal and logistical considerations related to study participation. Results will shape the development of future study design and methods, as well as recruitment strategy and educational resources to support the participant journey, from the first point of contact with the study.

3. Study Population:

Up to 3000 ***PPMI Clinical*** study participants in **the prodromal cohort** will be invited to participate in this study via the myPPMI online platform. These individuals may carry a gene variant related to PD, have hyposmia, and/or carry a diagnosis of REM Sleep Behavior Disorder. Participants in the prodromal cohort do not have a clinical diagnosis of PD at the time of study enrollment.

Inclusion Criteria

- Current PPMI Clinical study participant in the prodromal cohort
- Registered user of myPPMI
- Previously consented to be contacted regarding new research opportunities
- Internet connection
- Able to provide informed consent to participate

4. Recruitment and Informed Consent

Recruitment

PPMI participants who have agreed to be contacted regarding additional research opportunities, will be outreached via email. PPMI participants without an active myPPMI account will also be given the opportunity to create one, to take part in this study. The survey study will also appear as a new opportunity tile for eligible participants on their myPPMI homepage. Participants may also learn about this study from the PPMI study team, including The Michael J. Fox Foundation's community engagement team, the PPMI Site Management Core (SMC), and local site investigators and coordinators.

Informed Consent

Participants must be registered within myPPMI in order to complete the web-based survey. Individuals will have access to join this study via an opportunity tile surfaced on myPPMI. Participants will be asked to read and acknowledge an electronic informed consent document, prior to survey completion. Participants will have the opportunity to save a digital copy of the signed informed consent documentation for their records.

5. Study Activities

5.1. Study Procedures

After providing informed consent, individuals will be asked to complete a one-time web-based survey, with an estimated completion time of 20-30 minutes. Participants will be asked to complete the entire survey in one sitting but will be able to save their progress and complete the survey at a later time if they need to take a break for any reason.

A brief description of early intervention trials will be shared. The online survey will evaluate: 1) general interest in early intervention trials; 2) motivations for participation; 3) barriers to enrollment; 4) views on the risk-benefit balance of the trial; and 5) perceptions of logistical factors (e.g., random assignment, travel, drug delivery) associated with study participation. Participants will also provide basic demographic information, answer questions about their family and medical history and provide details about their experiences with PPMI to date. Survey questions were informed by the results of qualitative interviews conducted with 20 PPMI prodromal participants.

5.2. **Costs to the Subject**
Subjects will be responsible for any standard internet charges. There are no additional costs to the subject.

5.3. **Payment for Participation**
There is no payment for participation in this study.

6. Risks and Benefits of Participation

a) **Risks:** There is the risk of invasion of privacy and breach of confidentiality. While every effort will be made to maintain confidentiality, there is a small risk that information may be disclosed. However, safeguards are in place to reduce the risk of this happening. Data will be securely transferred between PPMI cores (designated study teams who collect, store, and handle study information) for the required workflows under the PPMI program. Any study data that is made available to researchers external to the PPMI study teams will be coded and will not contain identifiers.

There is also the risk of fatigue and emotional distress while completing the survey; however, participants may pause or stop the survey at any time. Educational resources related to brain health and well-being will be shared with participants after the survey; however, subjects will be advised to follow up with their physician should they experience any urgent health related issues.

b) **Benefits:** There is no anticipated benefit for participating in this study. However, participant feedback may improve our ability to successfully test new investigational treatments to slow or stop the development of Parkinson's disease.

7. Data Analysis

Descriptive statistics (e.g., frequencies, percentages, mode) will be calculated for each survey item. **Ordinal logistic regression** will model how factors like perceived benefits (e.g., potential to slow disease progression), concerns (e.g., side effects), and disease-related factors (e.g., severity of symptoms) influence interest in participation, controlling for demographic variables.
Subgroup analyses will explore how different demographic (age, gender, race/ethnicity, current PPMI site) and health-related characteristics (e.g., smell loss, RBD, family history of PD, PD gene) influence interest, motivations for participation, barriers to enrollment, views on risk-benefit ratio, and perceptions of practical and logistical considerations related to study participation.

8. PRIVACY AND CONFIDENTIALITY OF DATA

The Institute of Neurodegenerative Disorders (IND) has built and maintains the myPPMI platform. IND is committed to safeguarding participants privacy and personal data. The study team at IND

processes personal information as part of the PPMI study on behalf of The Michael J. Fox Foundation (MJFF). To protect participants personal information, IND has put in place procedures to secure the information processed, such as restricting access to collaborators and vendors as applicable to job function, logging and monitoring network activity, multi-factor authentication, and pseudonymization.

9. DATA SHARING AND STORAGE FOR FUTURE USE

Data collected for this study will be maintained and stored indefinitely across PPMI Cores including the Indiana University PPMI Cores (Indianapolis, IN), the Site Management and Data and Technology Cores at the Institute for Neurodegenerative Disorders (New Haven, CT), and the Statistical Core at the University of Iowa (Iowa City, IA) for conducting analyses as it pertains to the study including, but not limited to, enrollment and study outcomes. Data collected for this study will be incorporated into the PPMI database to create a fully harmonized PPMI database.

Study information will be accessed only by those who require access as it pertains to the individual's role in the study. All organizations responsible for data storage, or other collaborators or vendors of the PPMI study who may review study information, will observe the highest precautions to ensure data integrity and security.

All data obtained during the conduct of this study will be sent to the Laboratory of Neuro Imaging (LONI) in Los Angeles, California to be stored indefinitely for research purposes. Research data will be made available to researchers to conduct analyses related to PD and other disorders. Researchers will be required to comply with the PPMI data agreement to receive data. All personally identifiable information will be removed before it is shared outside the study.

REFERENCES

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