PROTOCOL

Title:	Parkinson's Progression Markers Initiative Online Study (PPMI Online)
Sponsor:	The Michael J. Fox Foundation for Parkinson's Research (MJFF)
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The Parkinson's Progression Markers Initiative Online Study (PPMI Online)

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1. PURPOSE OF STUDY

The Parkinson Progression Marker Initiative (PPMI) study is a longitudinal, observational, multi-center natural history study to assess progression of clinical features, digital outcomes, imaging, biologic, and genetic markers of Parkinson's disease (PD) progression in study participants with manifest PD, prodromal PD, and healthy controls. The overall goal of PPMI is to identify markers of disease progression for use in clinical trials of therapies to reduce progression of PD disability.

PPMI is a broad program that is expanding the goals of the original PPMI study[1], and will include this PPMI Online protocol, as well the PPMI Clinical, PPMI Remote, PPMI Digital Applications protocols (with external regulatory oversight). All participants in PPMI may be asked to participate in one or all of these protocols and their enrollment in these studies may occur in varying order. PPMI participants may also be asked to participate in additional PPMI companion studies (as they are developed), which may only involve a subset of PPMI participants based on their cohort designation. This protocol will be focused on the activities of the PPMI Online study (PPMI Online).

1.1 PRIMARY OBJECTIVE

The primary objective of PPMI Online is to collect participant reported health information from people with and without Parkinson's disease (PD), for the goal of better understanding risk and predictive factors for PD.

1.2 SECONDARY OBJECTIVE

Secondary objectives focus on the structural capabilities of PPMI Online, including:

1. Associating participant reported outcomes (PROs) provided in PPMI Online with data collected in the PPMI companion studies and Fox Insight study.
2. Identify best practice methods of recruiting and retaining participants and establish mechanisms to periodically evaluate recruitment methods.
3. Establish standardized protocols for acquisition, transfer, and analysis of health data that can be accessed by the PD research community for hypothesis generation, trend analyses, disease subset identification, and study recruitment.
4. Establish a platform amenable to companion protocols which can utilize the PPMI Online resources for purposes such as study recruitment and linking with PPMI protocols.
5. Establish a platform amenable to and a standardized protocol for sub-studies which integrate new surveys or other methods of data collection into the PPMI Online platform.

2. BACKGROUND AND RATIONALE

Characterizing symptom burden and disease course in people with PD has proved challenging, largely because of the wide variability in symptomatology. While in-person clinical evaluation has been the foundation of observational research, online evaluations

are increasingly important to reduce participant burden, ensuring continuity for participants too impaired to travel and enable access for the many people traditionally left out of academic research. Online evaluations can also reach a large number of people at minimal cost, allowing for broad recruitment and increasing representativeness of research cohorts. Similarly, while the in-person PPMI Clinical study will be an instrumental and core component to understanding the early development and progression of PD, evaluations through PPMI Online will provide further self-reported information about those with PD, as well as those in the broader PD community. Through PPMI Online, validated and exploratory PROs will supplement in-person evaluations and reach people unable to come into clinic. PROs will seek to describe the lived experiences of people with PD, identifying issues most relevant to patients, their care partners, and their family. The size and diversity of an online forum will allow detection of patterns among those without PD at risk of disease development and among those with PD at risk of poor outcomes. Self-reported outcomes through PPMI Online will therefore be an essential aspect of the broader PPMI initiative and ensure our understanding of PD is truly generalizable across the community and relevant to patients.

3. STUDY DESIGN

This protocol involves the indefinite, online collection of cross-sectional and longitudinal data from people with and without PD. The data will be collected through a web-based platform that can be continually modified and updated to accommodate study objectives and changes in the research environment over time. Once a participant registers for PPMI Online and agrees to participate, he/she will be asked to:

- Provide demographic and health history information (e.g., medical and medication history).
- Complete health-related questionnaires and surveys (e.g., questions related to PD and PD risk, daily activities, caregiving, and quality of life, etc.).
- Provide regular (approximately quarterly) updates to the self-reported information.
- Select participants will be invited to companion studies and have the option to consent to participate in the companion studies based on eligibility criteria.

4. STUDY POPULATION

This study will include people with and without PD. During the course of this study, we expect to enroll up to 500,000 participants globally.

5. RECRUITMENT METHODS

To achieve the recruitment goal, a multi-pronged approach will be employed, including (but not limited to) invitation to participate through PPMI studies, Fox Insight, independently managed PD studies, digital and social marketing recruitment efforts to the PD community, and through events or activities conducted by MJFF, or other representatives of PPMI.

The initial phase of PPMI Online will limit recruitment to participants living in the United states with eventual expansion to include participants globally.

6. PARTICIPANT ELIGIBILITY

Participants must meet the following criteria to enroll in PPMI Online:

6.1 Inclusion Criteria

6.1.1 Inclusion Criteria (PD Participants)

- Age 18 years or older
- Has received a diagnosis of Parkinson's disease
- Resides in the United States (initial phase only)

6.1.2 Inclusion Criteria (Participants without PD)

- Age 18 years or older
- Has not received a diagnosis of Parkinson's disease
- Resides in the United States (initial phase only)

7. OBTAINING INFORMED CONSENT

All potential participants interested in participating in the study will first create a user account including a user-name and password to register on the PPMI Online web portal. Following the creation of the user account, the participant will answer a brief screener questionnaire and then, if eligible, be brought to the informed consent page, where they will be required to read the consent on-line. If the individual consents to participate, they will acknowledge consent electronically using Evidation Health's eConsent process. Participants will be emailed a PDF copy of the signed consent and a PDF copy of the signed consent will be available on the study dashboard throughout the study.

8. PARTICIPANT ID ASSIGNMENT

A Participant ID number will be assigned to all PPMI Online participants. Participants will be assigned a 6-digit ID number generated automatically by the electronic database capture (EDC) system. Individuals already participating in another study under the PPMI program will retain the participant ID number previously assigned under that study. The PPMI Participant ID number will be used to identify a participant on all study related documentation.

9. STUDY PROCEDURES

PPMI Online is an online platform for people with and without PD that administers PROs remotely. Questionnaires are available for completion regularly at quarterly intervals. PPMI Online will incorporate a variety of PRO assessments throughout the study period, including addition of new questions or assessments.

Using standardized self-report questionnaires at baseline, the participants will be asked to provide their contact information. In addition to providing their personal contact information, each participant will be asked to provide the names, relationship to the participant and contact information for up to three designated informants who will serve as alternate contacts.

Participants may be invited to participate in additional PPMI Program studies at any time during their participation in PPMI Online, and if interested, will be fully informed about these studies and asked to provide separate consent prior to participating.

Participants will not be required to answer any questions they do not want to answer. The assessments and questionnaires fall under the following general categories, with individual assessments separately approved as PPMI Online study content:

Categories of Study Assessments:

- **Demographic and Vital Statistics:** Basic demographic information to describe the participant including but not limited to gender, race, education level, income, partner status, name, birth date, city and country of birth, and sex at birth. This information provides baseline characteristics among the participant groups and can be updated by the participant during the course of the study.

- **Medical and Family History:** A baseline medical history of the participant including Parkinson's status, surgical and medication history, as well as information about familial medical conditions. Participants can update this information over the course of the study period.

- **Conditions:** Participants will be able to report on new or continuing medical conditions that may occur during study participation.

- **Daily Living:** Information will be collected regarding various activities of daily living to understand what participants are experiencing over time and what changes may occur in their ability to complete those activities.

- **Symptoms:** Participants will provide information regarding signs and symptoms they are experiencing that relate to PD, other disorders, and other information about those symptoms such as severity and frequency.

- **Other:** Ancillary surveys or questions may be administered throughout the study period about, but not limited to, symptoms, disease progression, quality of life, care-partner experience, or general health of the study population. Surveys related to participant motivation for study participation, as well as the participant experience, may also be administered throughout the study period.

10. RISKS TO PARTICIPANTS

The most common risk associated with the online data collection is that study participants may feel anxious about completing the study tasks. There is a risk of disclosure of private information by participating in this study. However, safeguards are in place to reduce the risk of this happening. The full dataset, inclusive of identifiable data, collected for this study will be maintained electronically in secure databases, that have undergone security reviews, and with access limited to the study team and data management partners. Data may 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 are made available to researchers external to PPMI will be coded and will not contain identifiers. While every effort will be made to maintain confidentiality, there is a small risk that information may be disclosed. There may be other privacy risks

that the study team may have not foreseen.

11. POTENTIAL BENEFITS TO PARTICIPANTS

There are no direct anticipated benefits to study participants in this study. However, new information may be generated by the study to support development of better treatments for Parkinson's disease.

12. COSTS FOR PARTICIPATION

There will be no cost to the study participant for participating in this study.

13. PARTICIPANT WITHDRAWALS

Study participants will be informed during the consent process that they have the right to withdraw from the study at any time without prejudice. Withdrawal from this study may affect the study participant's continued participation in other PPMI studies as applicable to the companion study eligibility. Any information that has already been collected prior to the study participant's withdrawal will not be removed.

14. ADVERSE EVENTS

There will be no adverse event reporting as part of this online survey study. All data collected as part of this study are for research purposes only and not for clinical care purposes. There will not be any routine medical monitoring of the data collected nor any reports run looking at trends and/or worsening of a participant's condition requiring medical intervention.

15. PRIVACY AND CONFIDENTIALITY

Privacy of participants will be protected in that each person will have the option to voluntarily choose whether to participate in this study. The information being collected will be outlined during the consent process. Due to the remote nature of this study, participants will have the ability to determine when and where they complete the various assessments to maintain their privacy.

16. DATA SHARING AND STORAGE FOR FUTURE USE

Participant data collected for this study will be maintained and stored indefinitely at the PPMI study cores on secure, password protected systems. All identifiable study data will be accessed only by those who require access as pertains to the individual's role on the study. All organizations responsible for data storage and review will observe the highest precautions to ensure data integrity and security.

Data collected for this study will be maintained and stored indefinitely at the study cores and may be transferred and shared across participating PPMI for conducting analyses as pertains to the study including, but not limited to, enrollment, compliance, study outcomes and, in combination from the data received from PPMI Clinical, PPMI Online, PPMI Remote and companion studies studies, to enable modifications to the predictive prodromal eligibility criteria. All PPMI program data will be incorporated into the PPMI database to create a fully harmonized PPMI database.

All personally identifiable information will be removed and replaced with a Participant ID number to create coded study data. Coded 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. Coded 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.

17. ANALYSIS PLAN

On a regular basis, summary data will be reviewed to verify the completeness of the collected data. Based on this regular review recommendations may be made regarding modifications to the type of data collected and/or the data collection process. Recruitment and retention metrics will be regularly assessed by demographics characteristics overall and by cohort.

18. REFERENCES

1. Parkinson Progression Marker I. The Parkinson Progression Marker Initiative (PPMI). Prog Neurobiol 2011;95(4):629-635