FOLLOWUP OF PERSONS WITH NEURODEGENERATIVE DISEASES (FOUND) in the PARKINSON'S PROGRESSION MARKERS INITIATIVE (PPMI)

FOUND in PPMI

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1. PROTOCOL SYNOPSIS

Protocol Title	Follow-Up of Persons Participating in the Parkinson's Progression Markers Initiative
Acronym	FOUND in PPMI
Principal Investigator	Caroline M. Tanner, M.D., Ph.D. University of California-San Francisco (UCSF), San Francisco, CA
Study Centers	PPMI study sites in US, Europe, Israel and Australia (approximately **35** study sites)
Study Period	Indefinite
Primary Objective	To implement an efficient method for maintaining continuing contact with participants in the PPMI study, using easily sustainable methods
Study Population	PPMI study participants
Study Design	Prospective follow up using internet-based, mailed and/or telephone interviews **A. Enrollment:** PPMI participants will be enrolled into the FOUND protocol through these activities: 1) PPMI site staff briefly describe and determine each subject's willingness to learn about the FOUND in PPMI study 2) Interested PPMI participants provide contact information to PPMI staff at each site 3) PPMI staff provide participant contact information to the FOUND in PPMI staff 4) FOUND in PPMI staff contact PPMI participants electronically and/or by telephone and provide information regarding the study, discuss the consent form and answer any questions 5) PPMI participants s willing to enroll in the FOUND protocol sign the consent form and return it to FOUND in PPMI staff 6) FOUND in PPMI staff initiate regular follow-up contacts **B. Follow-up every 6 - 12 months:** Information collected at follow up includes contact information (address, email, telephone, and secondary contact persons), diagnosis, and information on health and disease status.
Number of Participants	~100,000 participants enrolled in PPMI
Main Eligibility/ Exclusion Criteria	<u>Inclusion Criteria</u> 1. Current or former participant in PPMI 2. Consent to participate in FOUND in PPMI

2.0 Background

The Follow-Up of Persons with Neurologic Disease (FOUND) protocol provides a parallel system for prospective follow up of persons with parkinsonism, related disorders and healthy controls participating in clinical research studies, complementing in-person assessment and enhancing retention (Tanner, 2014). FOUND provides centralized follow up for current and former participants in a clinical study, using methods convenient to the participant (e.g., internet, regular mail or telephone contacts) to systematically collect prospective information on each participant. FOUND provides immediate benefits that facilitate study conduct and improve study integrity. These include 1) minimizing lost-to-follow-up status for unanticipated dropouts during active participation in the primary in-person study, 2) providing continued assessment of disease status for those unable to complete the in-person study protocol, 3) providing systematically collected information on PPMI participants after completion of the in-person study, and 4) simplifying communications with current and former participants through use of a single IRB (centralized IRB).

In addition to these short-term benefits, the long-term benefits of FOUND take advantage of the intensive, high quality assessments conducted during the primary in-person study, and build on these to provide invaluable longitudinal information regarding PD natural history, long-term outcomes, treatment, and atypical features. Continued follow-up of former clinical study participants also provides a well-characterized cohort for testing new hypotheses (e.g., determinants of progression or adversity, disease subgroups).

The Parkinson's Progression Markers Initiative (PPMI) is a prospective longitudinal study involving persons with Parkinson's disease (PD), healthy controls and persons at risk for PD (Marek, 2011). The overall goal is to identify biomarkers of disease onset and progression in PD. Subjects were first enrolled in 2010. To date an estimated 670 of an expected 2000 persons have enrolled. Regular clinical assessments include assessment of PD, imaging and collection of blood, urine and CSF for biomarkers. The PPMI study is funded by the Michael J Fox Foundation. The principal investigator is Kenneth Marek, M.D., at the Institute for Neurodegenerative Disorders, New Haven, Connecticut. Study coordination is performed by the Clinical Core at the Clinical Trials Coordination Center at the University of Rochester, where the PPMI clinical database is maintained. Participants are enrolled at 35 sites internationally. Each site provides data to the Clinical Core using secure electronic data entry. De-identified data are provided to the PPMI Informatics Core at the Laboratory of Neuro Imaging (LONI) in Los Angeles, California, at regular intervals. De-identified data are shared with research scientists (see www.ppmi-info.org).

The University of California-San Francisco will conduct the FOUND in PPMI study. FOUND in PPMI is designed to enhance retention and minimize lost to follow-up of persons enrolled in PPMI, by providing a parallel longitudinal assessment method using internet, telephone and/or mail contacts with PPMI participants. This will be conducted through a single site, UCSF, and PPMI participants will provide consent to be followed in FOUND in PPMI separately. In this way, should a site no longer be able to participate, contact with PPMI participants enrolled at that site would be retained. In addition, if individual PPMI participants cannot continue in-person assessments, contact can be continued using FOUND in PPMI. FOUND in PPMI can also provide a method for providing information to study participants, and serve as a platform for continued follow-up.

3.0 Specific Aims

We propose to enroll PPMI participants into FOUND in PPMI. Our primary goals will be:

1. To maintain contact with participants in PPMI. This will be achieved by maintaining regular contact with participants, approximately every 6 – 12 months, and identifying two alternative contacts for each participant.
2. To determine if there is a change in clinical or vital status. This will be achieved by questionnaire and/or interviews of participants or their contacts.

To achieve these aims, enrolled PPMI participants will be contacted regularly, approximately every 6-12 months, using the FOUND protocol via internet, telephone and/or mail.

4.0 Participant Inclusion/Exclusion Criteria

All active participants in PPMI will be eligible to participate. In addition, individuals who have previously participated in PPMI, but are no longer participants will be eligible to participate.

5.0 Enrollment

5.1. PPMI Clinical Site Activity: Determine willingness to be contacted to learn about FOUND in PPMI**:** PPMI participants will be informed of the FOUND in PPMI remote follow-up protocol at an in-person PPMI assessment. For those persons who are no longer participants in PPMI, but who indicated willingness to be contacted for future research, study staff at the clinical site will contact the person by telephone or mail to provide information about the FOUND in PPMI protocol. Current and former PPMI participants will be asked if s/he is willing to be contacted to discuss the FOUND in PPMI follow-up protocol. Subjects will be informed that they will be asked at annual visits in the event they wish to decline at that time or delay their decision. Subjects choosing early withdrawal from

PPMI who have not enrolled in FOUND in PPMI will be offered the opportunity to enroll in FOUND in PPMI at the time of withdrawal. Participants who are willing to discuss the FOUND in PPMI protocol will provide contact information to the clinical site staff. Each subject's contact information will be sent to the FOUND in PPMI staff at UCSF, using a secure electronic or faxed contact form.

5.2 UCSF FOUND in PPMI Enrollment Methods: Each participant will be contacted by UCSF staff using email, telephone or postal mail, in accordance with the participant's preference.

5.2.a Electronic enrollment protocol: Individuals who wish to learn more about the FOUND in PPMI protocol and who are able to use the electronic data collection method will be provided materials explaining the study in an initial email. The study consent documents will follow in a second email generated by the DocuSign system. Former and current PPMI participants who agree to the terms of the study will be able to sign the informed consent form (IC), using secure methods via DocuSign. Participants who indicate that they have questions will not be able to sign the consent form, and will be asked to provide contact information so that the questions can be addressed. All questions regarding the FOUND in PPMI protocol will be answered by the FOUND in PPMI staff either by e-mail or telephone. After their questions have been addressed, persons who are willing to participate will again be directed to the website in order to sign the consent form. Follow up thereafter will be conducted primarily via online methods, although in some cases mailed information or telephone contact may be used. Similar methods have been used successfully in PPMI to identify and enroll individuals interested in PPMI (the Widespread Recruitment Initiative for persons at genetic risk for PD, conducted by Indiana University, see www.ppmi-info.org).

5.2.b Mail and telephone enrollment protocol: Potential participants who do not have access to email will be contacted by mail and telephone. FOUND in PPMI staff will contact each person by telephone and explain the study purpose and procedures. Following this call, interested persons will receive written materials explaining the FOUND in PPMI protocol, and a consent form. After the materials have been received, FOUND in PPMI staff will telephone in order to answer any questions and to review the consent form. Persons willing to participate will sign the consent form and return it by mail to UCSF. After the signed consent form is received, FOUND in PPMI staff will begin regular follow up. This method has been used successfully to provide informed consent to follow-up former clinical trials participants using the FOUND protocol (Tanner 2014).

6.0 Study Procedures

6.1 Baseline Assessment: At baseline, the subject will be asked to provide contact information, including email addresses, mailing addresses and telephone numbers. Each subject will be asked to provide the names, relationship to the

participant and contact information for two designated informants who will serve as alternate contacts. Additional subject information collected will include: date of birth, gender, social security number (to facilitate death records searches), neurologist (name, contact information) and permission to contact, primary physician (name, contact information) and permission to contact, current diagnosis (if any), current anti-parkinsonian medications, other health status.

6.2 Follow-up Assessments: At 6 – 12 month intervals, participants will be contacted by email, post or telephone. Each follow-up assessment will verify contact information, and request corrections for inaccurate information. Vital status, clinical status (diagnosis) and other clinical information will be collected. For those using the study website, the follow up data will be collected through the study website using secure online survey tools designed in REDCap. For those who are unable to use the study website, the follow up questionnaire will be mailed to the subject, including a postage paid return envelope.

6.3 Data Management: Data will be collected using the Research Electronic Data Capture (REDCap) system (https://redcap.ucsf.edu). Data will be stored on secure, password protected HIPAA-compliant servers hosted by the UCSF Data Center, with daily back up. REDCap is a secure, web-based database management tool, which is hosted by University of California-San Francisco Information Technology Services. REDCap has been developed for researchers collecting clinical research data, including protected health information (PHI). Participants will be able to directly enter responses to study questionnaires. Information from telephone interviews and mailed questionnaires will be data-entered by FOUND in PPMI staff members at UCSF using REDCap. All FOUND in PPMI staff will have university-approved security training and passwords regulating the level of data access. Staff with access to PHI will have additional training. PHI will be encrypted. Paper files containing PHI will be stored in locked file drawers in a secure environment. After editing and query resolution, paper files will be scanned and stored electronically, and the original files will be securely destroyed using UCSF services for documents containing PHI. The UCSF Data Center maintains a high level of data security, including rigorous security protection of the physical site, firewalls, updates of software, virus and spyware protection.

6.4 Data Transfer: De-identified data will be provided to the Informatics Core at the Laboratory of Neuro Imaging (LONI) in Los Angeles. Data provided to LONI may be shared with other researchers.

7.0 Adverse Events

In the unlikely event of a security breach or other adverse event associated with FOUND in PPMI, the event will be reported to the UCSF CHR within 5 working days of notification. The Michael J. Fox Foundation will also be informed of any adverse events associated with FOUND in PPMI.

8.0 Study Withdrawal/Discontinuation

Participation in this research project is completely voluntary. Subjects may withdraw at any time by notifying FOUND in PPMI staff by email, telephone conversation or post.

9.0 Statistical Considerations

The primary aim of this study is to retain PPMI participants. We will use descriptive statistics to report enrollment and follow-up results and subject characteristics. We will compare characteristics of participants enrolled and retained in FOUND in PPMI to those in PPMI but not in FOUND in PPMI using χ^2 and t-tests. To assess validity of self-reported diagnostic and clinical information, we will compare FOUND in PPMI self-reported information to analogous information collected at the temporally closest in-person PPMI visit (defined as the "gold standard"), using exact agreement, Spearman's correlation coefficients and kappa coefficients. To assess factors associated with retention, odds ratios will be calculated using multivariable logistic regression.

10.0 References

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