PPMI Publication Policy and Plan

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The Institute for Neurodegenerative Disorders

Genetic Kickoff Meeting
Sept 16, 2013
New York, NY
Goals-

High quality, rapid publication

Consistent with the broad PPMI collaboration
   SC, Cores, Sites, Working Groups

Credit PPMI investigators

Encourage non-PPMI community
Publication Policy

• Key Primary and Primary
• Others
• Abstracts for meetings
• Role of DPC
**Key Primary Publications** - *Key Primary Publications* are defined as those reports, analyses and publications identified by the PPMI Steering Committee as fulfilling the primary objectives of the study. Examples of these reports include publications detailing the baseline or yearly data-cuts

The SC will be primarily responsible for completion of all Key Primary Publications. Key Primary publications will be authored by the Steering Committee, Investigators, Study Cores and Working Groups reflecting the contribution of those authors.
For KEY primary publications

“And The Parkinson’s Progression Markers Initiative*” will be written on the author line of the manuscript with an asterisk referring to the list of names of individuals identified on the PPMI author list. The author list must be included as an appendix to ensure that all authors may be cited. The complete list of PPMI Study Investigators can be found at [www.ppmi-info.org/Authorslist](http://www.ppmi-info.org/Authorslist)

Sent to both the PPMI Steering Committee and the PPMI Data & Publications Committee (DPC) for review prior to journal submission.
Primary Publications - Primary publications are defined as reports, analyses and publications that are initiated by PPMI study members that utilize PPMI data, but which do not address the primary objectives of the study. Examples of these studies include a focus on specific biomarkers of disease progression, study infrastructure or recruitment.

Publications developed by study investigators, cores, working groups and authorship will reflect the contribution of those authors. In addition to the authors, “And The Parkinson’s Progression Markers Initiative*” will be written on the author line of the manuscript with an asterisk referring to the list of names of individuals identified on the PPMI author list. The author list must be included as an appendix to ensure that all authors may be cited. The list of PPMI Study Investigators can be found at www.ppmi-info.org/Authorslist
Primary Publications - Sent to both the PPMI Steering Committee and the PPMI Data & Publications Committee (DPC) for review prior to journal submission
Other Publications - It is expected that investigators outside of the study will conduct research and seek to publish analyses using PPMI data and specimens. These individuals are encouraged to publish novel scientific findings that result from their research using PPMI. Authorship of such a publication will not include PPMI in the author line,
PPMI personnel and PPMI funding support will be acknowledged by including the following within the manuscript:

"Data used in the preparation of this article were obtained from the Parkinson’s Progression Markers Initiative (PPMI) database (www.ppmi-info.org/data). For up-to-date information on the study, visit www.ppmi-info.org.”

“PPMI – a public-private partnership – is funded by the Michael J. Fox Foundation for Parkinson’s Research and funding partners, including [list the full names of all of the PPMI funding partners found at www.ppmi-info.org/fundingpartners ].”
All other publications must be sent to the PPMI DPC for administrative review prior to journal submission. To submit to the DPC, please upload the publication for review via the PPMI website.
Publication process - Primary

• Authors should develop data analysis plan in collaboration with Stats
• Authors should develop time-line for drafts and completion of report
• Goal is to identify authors for primary publications.
Source and Cut of Data

- Source should be LONI data so need to submit all data
- Timing of Data cuts - Data cuts to be published by SC
  - Baseline, 6 months, 1 year, then yearly
- Definition of full data set
Publication and Analysis plans
# Baseline data Papers

<table>
<thead>
<tr>
<th>Paper #</th>
<th>Description</th>
<th>Contact</th>
<th>Status</th>
<th>Date of Most Recent Change to List</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Overall Baseline Paper</td>
<td>Ken Marek</td>
<td>Preliminary Tables Reviewed</td>
<td>24 Apr 2013</td>
</tr>
<tr>
<td>2</td>
<td>Cognitive Paper</td>
<td>Dan Weintraub</td>
<td>Building Tables with Data</td>
<td>18 Apr 2013</td>
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<tr>
<td>3</td>
<td>DATSCAN Paper</td>
<td>John Seibyl / Ken Marek</td>
<td>Tables Sent to John and Ken / Feedback Pending</td>
<td>18 Apr 2013</td>
</tr>
<tr>
<td>4</td>
<td>DTI Paper</td>
<td>Norbert Schuff</td>
<td>-</td>
<td>24 Apr 2013</td>
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<tr>
<td>5</td>
<td>Biologics Paper</td>
<td>Les Shaw / John Trojanowski</td>
<td>-</td>
<td>18 Apr 2013</td>
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<tr>
<td>6</td>
<td>Urate Paper</td>
<td>Constantinescu Radu</td>
<td>Tables for an abstract sent to Radu / Feedback Pending</td>
<td>18 Apr 2013</td>
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Baseline data

- Primary baseline
- Subsets
- Cognitive – domains, compare UPDRS
- Imaging - DAT, AV133, DTI, Resting state
- Biologics - CSF analytes, Urate, Genetics
- Process - Recruitment, Imaging, CSF
- Ancillary - Tap
- SWEDD
ANALYSES

- TD vs PIGD
- Meds vs no Meds
- Comparison cognitive with imaging/CSF
- Sleep assessments
- Enrollment/recruitment
- Comparison of DAT and DTI
- UPDRS vs cognitive measures
Planned Analysis #1: Comparison of Baseline Characteristics Among Healthy Subjects and PD Subjects.

- Continuous variables assessed using t-test
- Dichotomous variables assessed using chi-square test
- Appropriate assumptions will be assessed for each comparison and any necessary adjustments (i.e., transformations) will be made prior to analysis
12 month data

- Primary baseline
- Subsets
- Cognitive – domains, compare UPDRS
- Imaging - DAT, AV133, DTI, Resting state
- Biologics - CSF analytes
- Process – Retention, CSF
- Ancillary - Tap
- SWEDD
Planned Analysis #2: Comparison of Short-Term Change in Progression Endpoints.

- Examine short-term change during first six months for each progression endpoint using mixed model (continuous endpoints) or logistic regression (dichotomous endpoints)
- Initial model will include all baseline characteristics, indicator for whether healthy control of PD patient, and all possible two-way interactions
- Will utilize backwards selection to build a model for each progression endpoint
Planned Analysis #3: Examination of Whether Short-Term Change in Progression Endpoints is Predictive of Change in Long-Term Endpoints

➤ Consider only progression endpoints that show differences between healthy subjects and PD patients

➤ Primary focus on long-term change in UPDRS score – additional long-term endpoints may be considered as well

➤ Ten-fold cross-validation procedure will be used to test predictive validity of each model

➤ If successful, final model will provide subset of short-term progression endpoints predictive of change in long-term endpoints – suggest biomarkers for future studies of interventions in PD patient populations
Planned Analysis #4: Examination of PD Subsets

- Each of first three sets of analyses will be repeated comparing subsets of PD patients
- If successful, final model will determine whether some short-term progression endpoints are more predictive of long-term endpoints for some subsets of PD patients and less predictive for other subsets
Planned Analysis #5: Proportion of SWEDD subjects that have a change in diagnosis over 24 month evaluation period

- Percentage and 95% confidence interval will be reported
- Other possible diagnoses will be further divided into 2 categories:
  - Other parkinsonian syndrome with a dopamine transporter deficit
  - Other condition with a dopamine transporter deficit
Planned Analysis #6: Exploratory analysis of SWEDD subjects

- Important changes over time found in planned analyses 1-3 will be assessed in the SWEDD subjects
- Will help to assess whether changes over time in SWEDD subjects are similar or dissimilar to PD subjects
Baseline

Tabulate and compare for all subjects Demographics by diagnostic category (PD, HC, SWEDD; Compare PD vs HC; PD vs SWEDD)

- Age
- Gender
- Education
- Ethnicity
- Race
- Family history of PD

(From tables 3 and 4 – monthly)
Baseline

Tabulate and compare for all subjects Summary clinical scores by diagnostic category (PD, HC, SWEDD; Compare PD vs HC; PD vs SWEDD)

- UPDRS Total and subscore
- Hoehn and Yahr
- Schwab and England
- Dur of Dis
- MOCA total
- GDS Total
- SCOPA AUT total
- State Anxiety
- QUIP
- UPSIT
- Epworth

(From tables 4 and 5)
Baseline

Tabulate and compare for all subjects DAT imaging SBR by diagnostic category (PD, HC, SWEDD; Compare PD vs HC; PD vs SWEDD)
- Mean striatal
- Mean putamen
- Mean caudate
- Ipsilateral Caudate
- Contralateral Caudate
- Ipsilateral Putamen
- Contralateral Putamen
Tabulate and compare for all subjects CSF synuclein, amyloid, Tau by diagnostic category (PD, HC, SWEDD; Compare PD vs HC; PD vs SWEDD)

- Aβ₁₋₄₂ (pg/mL)
- t-tau (pg/mL)
- p-tau₁₈₁ (pg/mL)
- t-tau/Aβ₁₋₄₂ ratio
- p-tau₁₈₁/Aβ₁₋₄₂ ratio
- p-tau₁₈₁/t-tau ratio
- A-syn (pg/mL)

Should we include hemoglobin data?
Baseline

UPDRS as an anchor: relationship between baseline UPDRS with non-motor, imaging, biologic at baseline (PD, HC, SWEDD; Focus on PD) – See Ravina et al. *Dopamine Transporter Imaging Is Associated With Long-Term Outcomes in Parkinson’s Disease*

Adjusted for age, gender, duration of disease

To be compared

MOCA total
GDS Total
SCOPA AUT total
State Anxiety
QUIP
UPSIT
Epworth
DAT
Aβ_{1-42} (pg/mL)
t-tau (pg/mL)
p-tau_{181} (pg/mL)
t-tau/Aβ_{1-42} ratio
p-tau_{181}/Aβ_{1-42} ratio
p-tau_{181}/t-tau ratio
A-syn (pg/mL)
PLANNED ANALYSES

Baseline

DAT scan as anchor: relationship between baseline DAT with motor, non-motor biologics at baseline (PD, HC, SWEDD; Focus on PD)  See Ravina et al. *Dopamine Transporter Imaging Is Associated With Long-Term Outcomes in Parkinson’s Disease*

Adjusted for age, gender, duration of disease

To be compared

- UPDRS
- MOCA total
- GDS Total
- SCOPA AUT total
- State Anxiety
- QUIP
- UPSIT
- Epworth
- $\text{A}\beta_{1-42}$ (pg/mL)
- t-tau (pg/mL)
- $p$-tau$_{181}$ (pg/mL)
- t-tau/$A\beta_{1-42}$ ratio
- $p$-tau$_{181}$/A$\beta_{1-42}$ ratio
- $p$-tau$_{181}$/t-tau ratio
- A-syn (pg/mL)
- Urate