INVESTIGATOR MEETING AGENDA

Wednesday, 7 December 2016 at the Radisson Blu Hotel, Glasgow

10:30  Welcome Coffee

11:00  Project Update  Mr Callum Smith, University of Glasgow

11:15  Olfaction Results & Data Queries  Mr Michael Lawton, University of Bristol

11:45  Parkinson’s Families Project  Prof Huw Morris, University College London

12:15  Diagnosis of PD & Treatment Response  Dr Katherine Grosset, NHS GGC

13:00  Lunch

14:00  Parkinson’s Pain Study Update  Dr Monty Silverdale, Greater Manchester Neuroscience Ctr

14:15  Overview of New Study Website  Dr Donald Grosset, CI, NHS GGC

15:30  Meeting closes
Tracking Parkinson’s
The PRoBaND study

Callum Smith

December 2016

Study Progress up to Now

February 2012 (study start)

Original study (0-36 months)
Interim extension (42-54 months)

• 2011 recent onset participants recruited
• 256 young onset participants recruited
• Total 2270
Progress: Patients for Visit 8

- Consistent recruitment to the extension this year
- Average of 41 per month in 2016

Progress: Patients for Visit 9

- First V9s recruited in Glasgow in summer
- Should average double figures per month in 2017
Progress: Relatives

- Most relatives have been involved already: total 339 (target 860)
- Recruitment open until at least November 2017
- Relative follow-up visits to start in mid-to-late 2017

Extension: Common Queries (1)

IQ-CODE

- Please remind patients to bring a relative or friend with them if possible
- The test can be given to the patient to take away with them, to be completed at home, if this isn’t an option
- Alternatively, it can be completed over the phone

New Assessments Reminder

- Likelihood of Diagnosis and Dyskinesia Rating Scale
Funding

- Claims for V8/9 funding made via Tracking Parkinson’s website

- Frequency of payment varies by site, mainly according to patient volume

**Reminder:**

- £73.55 for a V8
- £169.30 for a V9

Full Extension

February 2012 (study start)

1 2 3 4 5 6 7 8 9 10 11

Original study (0-36 months) Interim extension (42-54 months) Full extension (72-90 months)

- Ethics submitted; approval likely to be early next year

- Visits move to 18-month intervals: Visit 10 at 72 months (6 years) and Visit 11 at 90 months (7 and a half years).

- Content will follow the established format; we will send out new consent and information sheets once approval is granted.
New Journal Articles

- Malek et al., 2015. “Tracking Parkinson’s: Study Design and Baseline Data.”

- Swallow et al., 2016. “Statins are underused in recent-onset Parkinson’s disease with increased vascular risk: findings from the UK Tracking Parkinson’s and Oxford Parkinson’s Disease Centre (OPDC) discovery cohorts.”

- Malek et al., 2016. “Variation in recent onset Parkinson’s disease: implications for prodromal detection.”

- Malek et al., 2016. “Olfaction is Parkin single and compound heterozygotes in a cohort of young onset Parkinson’s disease patients.”

All can be found on PubMed and Google Scholar.

New Website

www.trackingparkinsons.org.uk

All old ClinBase functions are under the “Clinicians” tab.

These are mostly in the same format.

Participants will have the option to enter their own data for future visits.
Staff Changes

• I’m just beginning a PhD with Dr. Grosset

• Alison retiring March 2017

• Replacement staff to join us early 2017

Any questions, please ask
Tracking Parkinson’s

Harmonising olfaction tests

Michael Lawton

Measuring olfaction (sense of smell)

We have the problem that we measured olfaction in Tracking using two different tests. Started using the UPSIT (scored out of 40) and then switched to using the Sniffin’ Sticks test (scored out of 16).

To combine data on olfaction in our cohort we need to be able to convert scores on one test to scores on the other.

Also another PD cohort (OPDC Discovery cohort) used Sniffin’ Sticks to measure olfaction. Would be good to have a method that allowed the cohorts to be combined!
This table shows the UPSIT scores against the equivalent Sniffin’ scores. This enables us to take any UPSIT score and convert it into a Sniffin’ score.

<table>
<thead>
<tr>
<th>UPSIT score</th>
<th>Equivalent Sniffin’ sticks</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 4</td>
<td>0</td>
</tr>
<tr>
<td>5 - 6</td>
<td>1</td>
</tr>
<tr>
<td>7 - 8</td>
<td>2</td>
</tr>
<tr>
<td>9 - 10</td>
<td>3</td>
</tr>
<tr>
<td>11 - 12</td>
<td>4</td>
</tr>
<tr>
<td>13 - 14</td>
<td>5</td>
</tr>
<tr>
<td>15 - 16</td>
<td>6</td>
</tr>
<tr>
<td>17 - 18</td>
<td>7</td>
</tr>
<tr>
<td>19 - 21</td>
<td>8</td>
</tr>
<tr>
<td>22 - 23</td>
<td>9</td>
</tr>
<tr>
<td>24 - 25</td>
<td>10</td>
</tr>
<tr>
<td>26 - 27</td>
<td>11</td>
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<tr>
<td>28 - 30</td>
<td>12</td>
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<tr>
<td>31 - 32</td>
<td>13</td>
</tr>
<tr>
<td>33 - 35</td>
<td>14</td>
</tr>
<tr>
<td>36 - 37</td>
<td>15</td>
</tr>
<tr>
<td>38 - 40</td>
<td>16</td>
</tr>
</tbody>
</table>
We had a sample of 128 individuals who took both the UPSIT and Sniffin’ tests.

<table>
<thead>
<tr>
<th>Correlation between true score and converted equivalent score</th>
<th>Difference between scores mean (sd)</th>
<th>Difference between scores median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.80</td>
<td>0.14 (2.42)</td>
<td>0 (-1 to 2)</td>
</tr>
</tbody>
</table>

In this sample we can compare the true Sniffin’ scores to Sniffin’ scores converted from the UPSIT.

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**Tracking Parkinson’s Queries**

Michael Lawton
Corrections and outstanding/resolved status

When you correct online, please change Corrected on eCRF to “Yes”. Also please complete the Response (by study site) as well as correcting on the relevant eCRF. Sometimes I need to check the change made and it means I do not need to look in both the query centre and the corrected eCRF.

Feel free to change Status to “resolved” after answering and correcting. Although I keep a close eye on my queries and will change many to “resolved” myself.

Corrections and outstanding/resolved status

Maybe you can check if there are any outstanding queries at your centre? Or to be more specific any outstanding queries that have not been corrected online.
Which visit?

We now have about 50% of participants with data up to the 36 month visit. Many people have asked which visit does this query relate to? We have recently updated the query system so that the visit is included within the automatic email. Hopefully this will make things clearer.

For older queries (before this change was made in September 2016) you should be able to go into the review query system and find which visit it relates to. There may be some very old “outstanding” queries without the visit completed but I expect these are few.
Different Doses at different times?

What to do if an individual is on two different doses of medication at different times, for instance Ropinirole 4mg night time and 8mg during the day? Or pramipexole 0.18mg twice daily and 0.35mg once daily. The CRF is not designed to enter the data in that format.

![Image of medication doses]

In these instances it is not so important to know that they are on two different doses, we just need to know the total daily dose. So in the first example record dose as 12 and times per day as 1. Please also record the two different doses in the notes at the bottom of the eCRF.

Any questions? OR Suggestions?
What is a gene?
Outline

Genetics background
Family studies
PFP and progress
Therapy studies in pipeline

What do genes do?

DNA → transcription → RNA → translation → folding → amino acid chain → protein
Natural variation in the genome

Original DNA code for an amino acid sequence.

DNA bases:

C A T C A T C A T C A T C A T C A T C A T

Amino acid:

His  His  His  His  His  His  His

Replacement of a single nucleotide:

C A T C A T C A T C C T C A T C A T C A T

Incorrect amino acid, which may produce a malfunctioning protein.

U.S. National Library of Medicine

Many recent trials of new treatments have failed...

% remaining untreated

Years from diagnosis

- Normal course of Parkinson’s
- ‘disease modifying’ treatment
- recent trial results
LRRK2 G2019S is common and dependent on ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Sporadic</th>
<th>Familial</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>North African Arabs</td>
<td>39%</td>
<td>36%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Ashkenazi Jews</td>
<td>10%</td>
<td>28%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>UK British</td>
<td>1%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Welsh</td>
<td>0.3%</td>
<td>1.5%</td>
<td>NA</td>
</tr>
</tbody>
</table>

Healy 2008
LRRK2 penetrance


How genetic is PD? Autosomal Dominant Disease – Multiplex families

54 CANDAS multiplex cases (3 or more affected)
3 LRRK2 mutations
1 VPS35 positive
1 synuclein positive
1 PINK1 – pseudo-dominant
11% positive; 89% negative
Tracking Parkinson’s 1: Genetic factors

– GBA mutation 3%, variation in 6.8%
– LRRK2 0.7%
– PINK1 and Parkin <0.5% (only tested in young onset)
– GBA minimal cognitive differences at baseline, but significant excess of PIGD
– Exome analysis in process
Background

Inspired by Tracking/PROBAND!
Yoav Ben-Shlomo EOPD

Aims

• **Primary Aim**
• To identify genetic variants that predispose to or cause Parkinson’s disease/parkinsonism (PD).

• **Secondary Aims**
• To identify genetic factors that may influence the phenotype and clinical characteristics of PD
• To identify families that may be prepared to participate in translational research related to PD
Key Features

Consent

Relatives

Eligibility

Recruitment of Index cases and Relatives

Eligibility for index case:
Diagnosis of Parkinson’s disease or parkinsonism with either:
Age of onset <45 (early onset PD; EOPD), and/or
Family history of PD (FPD)

Eligibility for relatives:
Relative of index case, either affected or unaffected by PD.
Assessments

Study assessments follow the PRoBaND Tracking Parkinson’s assessments:
MDS-UPDRS Clinician assessment
Montreal Cognitive Assessment
Standardised questionnaires (PDQ8, EQ5D, ESS, RBD, HADS, QUIP, Constipation, SCOPA-AUT, MDS-UPDRS Patient, PDSS)
Life History questionnaire and MERQ-PD, including family history
Blood samples for DNA and peripheral blood lymphocytes (PBLs)
Review of medical records

Data entered to REDCAP database via secure survey links

PFP - What if you find something for PD?

If possible, I would like to be informed of research results that might indicate that an NHS (or equivalent) test could be developed or used, related to my condition, which might help me or my family - YES/NO

I am happy to be contacted by telephone or letter to obtain more information or about future research projects - YES/NO
PFP - What if you find something else (incidental findings)?

If possible, I would like to be informed of research results that might indicate that an NHS (or equivalent) test could be developed or used, unrelated to my condition, which might help me or my family. - YES/NO

Progress

240 participants have been recruited so far.
30 sites are currently active
10 sites are in development
41 samples have been sent for exome sequencing, with results expected over the next month
# Progress

<table>
<thead>
<tr>
<th>Percentage of all familial cases</th>
<th>Age of onset</th>
<th>Percentage of all early onset cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>One other family member affected</td>
<td>&lt;30</td>
<td>15.8%</td>
</tr>
<tr>
<td>Two other family members affected</td>
<td>≥30 - &lt;35</td>
<td>18.4%</td>
</tr>
<tr>
<td>Three other family members affected</td>
<td>≥35 - &lt;40</td>
<td>26.3%</td>
</tr>
<tr>
<td>Four or more other family members affected</td>
<td>≥40 - ≤45</td>
<td>39.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EOPD (n=26)</th>
<th>FPD (n=53)</th>
<th>EOPD and FPD (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS-UPDRS total</td>
<td>64.9 (30.4)</td>
<td>45.5 (24.8)</td>
</tr>
<tr>
<td>MDS-UPDRS Part 1</td>
<td>12.9 (7.6)</td>
<td>9.5 (7.1)</td>
</tr>
<tr>
<td>MDS-UPDRS Part 2</td>
<td>17.5 (10.2)</td>
<td>10.7 (7.8)</td>
</tr>
<tr>
<td>MDS-UPDRS Part 3</td>
<td>30.6 (17.2)</td>
<td>24.6 (14.0)</td>
</tr>
<tr>
<td>MDS-UPDRS Part 4</td>
<td>3.1 (4.2)</td>
<td>1.4 (2.2)</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr stage</td>
<td>1.8 (0.9)</td>
<td>1.6 (0.9)</td>
</tr>
<tr>
<td>MoCA total (max 30)</td>
<td>20.1 (11.5)</td>
<td>20.3 (11.2)</td>
</tr>
<tr>
<td>PDQ8 (max 32)</td>
<td>10.6 (7.1)</td>
<td>6.6 (5.8)</td>
</tr>
<tr>
<td>EQSD (max 15)</td>
<td>8.4 (2.0)</td>
<td>7.4 (1.9)</td>
</tr>
<tr>
<td>ESS (max 24)</td>
<td>8.7 (6.8)</td>
<td>6.9 (4.5)</td>
</tr>
<tr>
<td>RBD-SQ (max 13)</td>
<td>6.2 (3.2)</td>
<td>5.0 (2.9)</td>
</tr>
<tr>
<td>HADS anxiety (max 21)</td>
<td>7.1 (3.9)</td>
<td>4.8 (3.7)</td>
</tr>
<tr>
<td>HADS depression (max 21)</td>
<td>6.5 (3.8)</td>
<td>4.6 (3.5)</td>
</tr>
<tr>
<td>QUIP (max 13)</td>
<td>1.7 (2.2)</td>
<td>0.5 (1.1)</td>
</tr>
<tr>
<td>SCOPA-AUT (max 69)</td>
<td>16.4 (10.5)</td>
<td>13.0 (7.9)</td>
</tr>
<tr>
<td>PDSS (max 150)</td>
<td>95.1 (26.0)</td>
<td>102.2 (25.5)</td>
</tr>
</tbody>
</table>
Testing the right treatments in the right people

Therapy studies (linked to genetics)

Edison / Epi-589 (early onset PD – parkin) Morris, CPT

AIM-PD (GBA) Schapira, CPT

Kinase inhibitors (LRRK2 in development)

PD-STAT CPT, Pharmacogenomics

Exenatide CPT, Pharmacogenomics
Acknowledgements

Patients and Carers

Research Nurses and Practioners !!

International PD Genomics Consortium: Andrew Singleton, Nick Wood, Mike Nalls, Jose Bras

Tracking Parkinson’s: Donald Grosset, Nigel Williams

PFP: Manuela Tan, Sarah Cable Concetta Brugaletta Steven Lubbe

Funding and Support: Parkinson’s UK, UCL
Tracking Parkinson’s
The PRoBaND study

PD or not PD that is the question?

Diagnostic Accuracy

Katherine Grosset
How easy is it to diagnose PD?

PD or not PD?

**Degenerative**

- Idiopathic PD
- ‘Parkinson Plus’

**Non-degenerative**

- Essential tremor
- Dystonic tremor
- Drug-induced parkinsonism
- Vascular parkinsonism

‘Plus’ refers to involvement of other components of the nervous system:

**Multiple System Atrophy (MSA)**

- Parkinsonism
- + Cerebellum (Coordination)
- + Autonomic
  (Bladder, Blood pressure)

**Progressive Supranuclear Palsy (PSP)**

- Parkinsonism
- + Eye movements
- + Cognitive problems
Tracking Parkinson’s

The PRoBaND study

who did we recruit?

Inclusion and Exclusion criteria

Patient has completed informed consent: If answer is no, the case should not be entered into the study until consent has been obtained.

- Yes
- No

Patient has severe comorbid illness that would prevent full study participation: If answer is yes, the patient should NOT be entered into the study.

- Yes
- No

Patient has features indicating another degenerative Parkinsonism e.g. progressive supranuclear palsy: If answer is yes, the patient should NOT be entered into the study.

- Yes
- No

Patient has drug induced parkinsonism: If answer is yes, the patient should NOT be entered into the study, although drug unmasked PD is allowed - answer NO if this is the case.

- Yes
- No

Patient has symmetrical lower body Parkinsonism attributable to significant cerebrovascular disease (incidental small vessel disease is allowed): If answer is yes, the patient should NOT be entered into the study.

- Yes
- No

Negative or normal functional imaging of the presynaptic dopamine system: If answer is yes, the patient should NOT be entered into the study.

- Yes
- No

Tools to help us?

old
(1992)

new
(2015)
How easy is it to diagnose PD?

**Diagnostic Criteria for PD**

Having established that the patient has parkinsonism, the MDS-PD criteria will be applied to determine whether the patient meets criteria for PD as the cause of this parkinsonism.

**Diagnosis of clinically established PD requires:**

1. Absence of absolute exclusion criteria
2. At least two supportive criteria
3. No red flags

**Diagnosis of clinically probable PD can be made in:**

1. Absence of absolute exclusion criteria
2. Presence of red flags counterbalanced by supportive criteria, i.e., if one red flag is present there must also be at least one supportive criterion; if **two red flags** at least **two supportive criteria** are needed. If there are more than **two red flags**, clinically probable PD cannot be diagnosed.

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**Supporting Features**

**Exclusions/Red Flags**

1. Occlusion disturbsences
2. Exclusion disturbances (e.g., "spasm" of lid opening, blepharospasm)

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**PD Diagnosis & Treatment - Katherine Grosset**

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**How are we assessing diagnostic accuracy?**
Tracking Parkinson’s change in diagnosis

Not PD 1.6% - so far!

Unusual or Atypical Features – 8.4%
What happens when you apply different criteria?

Using the MDS criteria

• At baseline 11.2% of our cases did not fulfil MDS clinical diagnostic criteria for the diagnosis of PD
  • 27.6% clinically probable
  • 61.3% clinically established

Why were these cases categorised as not PD?
### Why are these cases “not PD”?

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All cases</th>
<th>Not PD</th>
<th>Clinically probable</th>
<th>Clinically established</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=2000 (11.2%)</td>
<td>N=223 (11.2%)</td>
<td>N=551 (27.6%)</td>
<td>N=1226 (61.3%)</td>
<td></td>
</tr>
</tbody>
</table>

### Absolute exclusion criteria

- Cerebellar: 25 (1.3%) Not applicable
- Gaze palsy: 117 (5.8%) Not applicable
- FT dementia/PPA: 0 (0.0%) Not applicable
- Lower limbs: 1 (0.1%) Not applicable
- Drug Induced: 2 (0.1%) Not applicable
- No l-dopa response: 72 (3.6%) Not applicable
- Cortical sensory: 8 (0.4%) Not applicable
- Normal DAT: 0 (0.0%) Not applicable
- Alternative cause parkinsonism: 0 (0.0%) Not applicable

### Are the cases classed as “not PD” different?

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All cases</th>
<th>Not PD</th>
<th>Clinically probable</th>
<th>Clinically established</th>
<th>Adjusted p-value Not PD vs Clinically probable</th>
<th>Adjusted p-value Not PD vs Clinically established</th>
<th>Adjusted p-value Clinically probable vs Clinically established</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=2000 (11.2%)</td>
<td>N=223 (11.2%)</td>
<td>N=551 (27.6%)</td>
<td>N=1226 (61.3%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Age onset**: 63.0 (9.8) vs 62.6 (9.6) vs 62.7 (9.8) vs 63.0 (9.7) p=0.94
- **Age Diagnosis**: 66.2 (9.3) vs 65.8 (9.4) vs 66.0 (9.3) vs 65.8 (9.3) p=0.82
- **Age baseline**: 67.6 (9.3) vs 67.2 (9.3) vs 67.2 (9.3) vs 67.2 (9.3) p=0.82
- **Disease duration**: 1.3 (0.5) vs 1.2 (0.5) vs 1.4 (0.5) vs 1.4 (0.5) p=0.007
- **Gender (Male)**: 1299 (64.9%) vs 152 (68.2%) vs 352 (63.9%) vs 795 (64.8%) p=0.35
- **Symptoms at onset**: Tremor: 1452 (71.4%) vs 145 (66.2%) vs 299 (57.6%) vs 1008 (83.0%) p=0.018
- **Bradykinesia**: 1405 (78.5%) vs 178 (83.2%) vs 390 (76.3%) vs 925 (78.6%) p=0.035
- **Postural instability**: 364 (19.8%) vs 65 (31.0%) vs 107 (21.4%) vs 192 (17.0%) p=0.003

### PD Diagnosis & Treatment - Katherine Grosset

PD Diagnosis & Treatment - Katherine Grosset
What happens with follow up?

- Baseline
  - 11.2% not PD
  - 27.6% clinically probable
  - 61.3% clinically established

- At 2½ years
  - 23.6% not PD
  - 24.0% clinically probable
  - 52.4% clinically established
What happens with follow up?

• Baseline
  • 11.2% not PD
  • 27.6% clinically probable
  • 61.3% clinically established

• At 2 ½ years
  • 23.6% not PD
  • 24.0% clinically probable
  • 52.4% clinically established

How does established become unestablished?

Follow up data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All cases</th>
<th>Not PD N=472 (23.6%)</th>
<th>Clinically probable N=480 (24.0%)</th>
<th>Clinically established N=1048 (52.4%)</th>
<th>Adjusted p-value Not PD vs Clinically probable</th>
<th>Adjusted p-value Not PD vs Clinically established</th>
<th>Adjusted p-value Clinically probable vs Clinically established</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age onset</td>
<td>64.4 [9.8]</td>
<td>65.5 [9.3]</td>
<td>64.9 [9.9]</td>
<td>63.7 [9.3]</td>
<td>0.45*</td>
<td>0.002*</td>
<td>0.031*</td>
</tr>
<tr>
<td>Age Diagnosis</td>
<td>64.2 [9.3]</td>
<td>67.5 [8.8]</td>
<td>60.9 [9.3]</td>
<td>65.5 [9.3]</td>
<td>0.49*</td>
<td>&lt;0.001*</td>
<td>0.005*</td>
</tr>
<tr>
<td>Age baseline</td>
<td>67.6 [9.1]</td>
<td>68.7 [8.6]</td>
<td>68.2 [9.6]</td>
<td>66.3 [9.3]</td>
<td>0.49*</td>
<td>&lt;0.001*</td>
<td>0.005*</td>
</tr>
<tr>
<td>Disease duration</td>
<td>1.3 [0.9]</td>
<td>1.3 [0.9]</td>
<td>1.4 [0.5]</td>
<td>1.3 [0.9]</td>
<td>0.50*</td>
<td>0.65*</td>
<td>0.23*</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>1299 (64.9%)</td>
<td>324 (68.6%)</td>
<td>306 (65.8%)</td>
<td>669 (63.8%)</td>
<td>0.12*</td>
<td>0.034*</td>
<td>0.10*</td>
</tr>
<tr>
<td>Symptoms at onset</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tremor</td>
<td>1452 (74.4%)</td>
<td>140 [50.6%]</td>
<td>190 [63.8%]</td>
<td>842 [81.8%]</td>
<td>0.039*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Rigidity</td>
<td>1327 (71.9%)</td>
<td>341 (75.3%)</td>
<td>217 [72.0%]</td>
<td>695 (73.2%)</td>
<td>0.63*</td>
<td>0.32*</td>
<td>0.65*</td>
</tr>
<tr>
<td>Bradykinesia</td>
<td>1403 (78.5%)</td>
<td>348 [77.0%]</td>
<td>764 [77.6%]</td>
<td></td>
<td>0.019*</td>
<td>0.003*</td>
<td>0.97*</td>
</tr>
<tr>
<td>Postural instability</td>
<td>564 (19.8%)</td>
<td>140 (27.3%)</td>
<td>109 [24.6%]</td>
<td>315 [14.2%]</td>
<td>0.30*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Motor Subtype</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tremor Dominant</td>
<td>832 (49.9%)</td>
<td>158 [50.6%]</td>
<td>163 [51.9%]</td>
<td>511 [50.7%]</td>
<td>0.58*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>PDGD</td>
<td>745 (45.1%)</td>
<td>122 [39.9%]</td>
<td>118 [31.9%]</td>
<td>305 [32.1%]</td>
<td>0.30*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>235 (13.0%)</td>
<td>20 [6.9%]</td>
<td>44 [14.7%]</td>
<td>195 [14.2%]</td>
<td>0.84*</td>
<td>0.41*</td>
<td>0.275</td>
</tr>
</tbody>
</table>
### Follow up data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All cases N=2000</th>
<th>Not PD N=472 (23.6%)</th>
<th>Clinically probable N=480 (24.0%)</th>
<th>Clinically established N=1048 (52.4%)</th>
<th>Adjusted p-value Not PD vs Clinically probable</th>
<th>Adjusted p-value Not PD vs Clinically established</th>
<th>Adjusted p-value Clinically probable vs Clinically established</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MoCA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1342 (73.2%)</td>
<td>300 (68.5%)</td>
<td>315 (71.3%)</td>
<td>727 (76.2%)</td>
<td>0.53d</td>
<td>0.017d</td>
<td>0.11d</td>
</tr>
<tr>
<td>MCI</td>
<td>227 (12.4%)</td>
<td>56 (12.8%)</td>
<td>52 (11.8%)</td>
<td>119 (12.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td>265 (14.4%)</td>
<td>82 (18.7%)</td>
<td>75 (17.0%)</td>
<td>108 (11.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>UPDRS 3</strong></td>
<td>22.9 (12.3)</td>
<td>25.1 (12.3)</td>
<td>22.9 (12.4)</td>
<td>21.9 (12.2)</td>
<td>0.013d</td>
<td>&lt;0.001d</td>
<td>0.47d</td>
</tr>
<tr>
<td>Hoehn and Yahr Stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1.5</td>
<td>948 (47.9%)</td>
<td>186 (39.7%)</td>
<td>236 (49.9%)</td>
<td>526 (50.7%)</td>
<td>&lt;0.001d</td>
<td>&lt;0.001d</td>
<td>0.62d</td>
</tr>
<tr>
<td>2-2.5</td>
<td>894 (45.2%)</td>
<td>224 (47.9%)</td>
<td>205 (43.3%)</td>
<td>465 (44.8%)</td>
<td>&lt;0.001d</td>
<td>&lt;0.001d</td>
<td>0.007d</td>
</tr>
<tr>
<td>3+</td>
<td>137 (6.9%)</td>
<td>58 (12.4%)</td>
<td>32 (6.8%)</td>
<td>47 (4.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated</td>
<td>196 (9.8%)</td>
<td>42 (8.9%)</td>
<td>58 (12.2%)</td>
<td>96 (9.2%)</td>
<td>0.093d</td>
<td>0.93d</td>
<td>0.034d</td>
</tr>
<tr>
<td>LEDD (mg/day)</td>
<td>294 (111)</td>
<td>322 (225)</td>
<td>286 (220)</td>
<td>286 (200)</td>
<td>0.002d</td>
<td>0.002d</td>
<td>0.62d</td>
</tr>
</tbody>
</table>

### PD or not PD?

- **Not PD**
  - Older
  - Gaze palsy
  - Less tremor
  - Higher UPDRS 3
  - More cognitive problems
  - Less L-dopa response

- **Established PD**
  - Younger
  - More tremor
  - Lower UPDRS 3
  - Less cognitive problems
  - Better L-dopa response
How does this tie into published studies?

26% of clinically possible and 82% of clinically probable had PD at autopsy.
7 of the 16 cases with no autopsy evidence of PD had PSP.

Change in diagnosis – would they have been included using the MDS Criteria?

MDS criteria category for cases with a change in diagnosis:

**Baseline**
- 8 not PD
- 10 probable PD
- 14 established PD

**Follow up**
- 14 not PD
- 7 probable PD
- 11 established PD

More exclusions and red flags emerge with time.
32 Change in diagnosis – what did the diagnosis change to?

- 4 SWEDDS (not degenerative dopaminergic condition)
  - 2 not PD
  - 2 established PD

- 28 (5 MSA, 4 PSP, 19 other – CBD, vascular, dystonic, unknown)
  - 4 not PD
  - 10 probable PD
  - 14 established PD

Supportive Criteria – response to dopaminergic therapy

Supportive criteria
(Check box if criteria met)

☐ 1. Clear and dramatic beneficial response to dopaminergic therapy. During initial treatment, patient returned to normal or near-normal level of function. In the absence of clear documentation of initial response a dramatic response can be classified as:
   a) Marked improvement with dose increases or marked worsening with dose decreases. Mild changes do not qualify. Document this either objectively (>30% in UPDRS III with change in treatment), or subjectively (clearly-documented history of marked changes from a reliable patient or caregiver).
Response to dopaminergic therapy – the L-dopa challenge

<table>
<thead>
<tr>
<th>L-Dopa Challenge test [using 30% response]</th>
<th>Positive</th>
<th>Negative</th>
<th>Adjusted p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variable</strong></td>
<td>Total N=996</td>
<td><strong>Positive N=510 (51.2%)</strong></td>
<td><strong>Negative N=486 (48.8%)</strong></td>
</tr>
<tr>
<td>Age baseline (yrs)</td>
<td>67.4 (9.1)</td>
<td>65.9 (9.5)</td>
<td>69.1 (8.4)</td>
</tr>
<tr>
<td>Age diagnosis (yrs)</td>
<td>66.1 (9.1)</td>
<td>64.3 (9.5)</td>
<td>97.7 (8.4)</td>
</tr>
<tr>
<td>Disease duration (yrs)</td>
<td>1.3 (0.9)</td>
<td>1.3 (0.9)</td>
<td>1.3 (0.9)</td>
</tr>
<tr>
<td>Male</td>
<td>677 (68.0%)</td>
<td>335 (65.7%)</td>
<td>342 (70.4%)</td>
</tr>
<tr>
<td>% response in L-Dopa challenge</td>
<td>31.1 (22.8)</td>
<td>48.5 (14.1)</td>
<td>12.8 (14.1)</td>
</tr>
<tr>
<td>LEDD (mg/day)</td>
<td>312 (195)</td>
<td>319 (202)</td>
<td>104 (188)</td>
</tr>
<tr>
<td>MDS UPDRS 3</td>
<td>22.4 (11.8)</td>
<td>20.5 (10.0)</td>
<td>24.3 (13.1)</td>
</tr>
<tr>
<td>Change in MDS UPDRS 3 from baseline to 18 months</td>
<td>4.4 (10.7)</td>
<td>2.8 (10.7)</td>
<td>6.0 (10.6)</td>
</tr>
</tbody>
</table>

- MoCA
  - Total Score: 25.6 (3.3) vs. 25.6 (3.2) vs. 25.5 (3.3) (p=0.29)
  - Normal: 713 (77.6%) vs. 373 (78.7%) vs. 340 (75.9%) (p=0.67)
  - MCI: 102 (11.1%) vs. 45 (9.6%) vs. 57 (12.7%) (p=0.36)
  - Dementia: 104 (11.3%) vs. 53 (11.3%) vs. 51 (11.4%) (p=0.64)
  - NMSS total: 32.8 (25.8) vs. 32.4 (24.3) vs. 33.2 (27.4) (p=0.27)
  - Hypomia: 625 (72.1%) vs. 337 (74.4%) vs. 288 (69.6%) (p=0.96)
  - RBD: 345 (36.7%) vs. 184 (37.9%) vs. 161 (35.4%) (p=0.39)
  - Constipation: 346 (35.6%) vs. 172 (34.2%) vs. 174 (37.0%) (p=0.97)
  - Depression: 213 (22.0%) vs. 108 (21.6%) vs. 105 (22.4%) (p=0.38)
  - SCOPA-AUT total: 12.1 (7.0) vs. 11.8 (6.8) vs. 12.5 (7.2) (p=0.28)
Response to dopaminergic therapy according to vascular risk and co-morbidity

- Vascular diagnosis
- QRISK2 ≥20%
- QRISK2 10-20%
- QRISK2 ≤10%

L-Dopa Challenge % Positive (n=510, 51.2%)  L-Dopa Challenge % Negative (n=486, 48.8%)

Response to dopaminergic therapy according to vascular risk and co-morbidity

- Hypertension
- High cholesterol
- Type 2 Diabetes
- Transient ischaemic attack/stroke
- Myocardial infarction
- Angina

L-Dopa Challenge % Positive (n=510, 51.2%)  L-Dopa Challenge % Negative (n=486, 48.8%)

PD Diagnosis & Treatment - Katherine Grosset
Tracking Parkinson’s:
original primary objective

• **Primary objective:** To define and explain the variation in the clinical phenotype of Parkinson’s disease.

• Meaningful subgroups
  • Which patients respond to L-dopa
  • Rate of progression

• Do the MDS criteria for diagnosing PD provide us with meaningful subgroups?
  • Clinically Established/Clinically Probable/Not PD

Tracking Parkinson’s
The PRoBaND study

PD or not PD that is the question?
PD or not PD that is the question?

- According to the MDS criteria
  - 24% are not PD

or

[Image of a meme saying, "IT'S PD JIM BUT NOT AS WE KNOW IT"]
or

Not PD
- Parkinson’s Plus
- Non degenerative conditions
- Vascular parkinsonism
- PD with co-morbidities

Tracking Parkinson’s: what have we achieved?

- Thanks to a massive effort from patients and you the research team to form a huge data set

- Clinically useful subgroups
  - Therapeutics
  - Phenotype
  - Progression
The Parkinson's Pain Study

Monty Silverdale
Consultant Neurologist
Greater Manchester Neuroscience Centre
Why do so many of my PD patients complain of pain?

Is it all just tissue damage due to mobility problems?
Hypothesis - pain in Parkinson's disease is mainly due to central sensitisation.
Parkinson's Pain Study

• What causes pain in Parkinson’s disease
• Is it mainly due to mobility factors?
• Is it mainly due to central sensitisation?
• How should we treat pain in PD?

Before funding 2012-2014

• Study at SRFT over 18 months
• 50 participants recruited
• Confirmed that chronic pain is common in PD – around 70%
• Poor correlation with mobility problems (suggests central sensitisation as the cause)
After Funding 2014-2016

- Study NIHR adopted
- Started using DeNDRoN research team
  - 2038 participants
    - 1462 Proband Study
    - 576 Oxford Discovery Study

"Well, yes I can see there's definitely potential for growth."

Pain Study - Monty Silverdale
Thanks for all your help

Initial Data

• 85% reported pain at time of assessment
• 40% moderate or severe pain (score 5 or more on VAS) regularly over past month
The next stage

- Combine with all the Proband data
- Combine with all the Oxford Discovery data
- Combine with the GWAS data
- Hope to finish over next few months
The Parkinson's Pain Study – the end

Monty Silverdale
Consultant Neurologist
Greater Manchester Neuroscience Centre

Tracking Parkinson’s (PRoBaND)
Updates to Web interface

Donald Grosset
Consultant Neurologist and Honorary Professor

December 2016
29.11.16 Site fully operational for Clinicians

Tracking Parkinson's is a UK-based study

The study is funded by Parkinson's UK

It has been running since 2011

There are over 2500 participants

Clinicians

Blood sample posting over Xmas 2016: Please do not post samples after December 16th

This section is for Clinical Study Centres. It is used to review and enter data at each site. After logging in (use your ClinBase details) you can access the same functions as before.

ClinBase Clinician Login
Enter login details

Username
Password
Centre

Login
Clinicians

Blood sample posting over Xmas 2016: Please do not post samples after December 16th

This section is for Clinical Study Centres.
It is used to review and enter data at each site.
After logging in (use your ClinBase details) you can access the same functions as before.

ClinBase Clinician Login
Enter login details

<table>
<thead>
<tr>
<th>Field</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Username</td>
<td>dgrosset7456</td>
</tr>
<tr>
<td>Password</td>
<td>**********</td>
</tr>
<tr>
<td>Centre</td>
<td>11</td>
</tr>
</tbody>
</table>

Login

Clinicians

Blood sample posting over Xmas 2016: Please do not post samples after December 16th

This section is for Clinical Study Centres.
It is used to review and enter data at each site.
After logging in (use your ClinBase details) you can access the same functions as before.

Make entries below, then click Submit

Email *
donaldgrosset@gmail.com

Choose an option from the list
- 1. Enter data for a case
- 2. View or edit data for a case
- 3. Overview - cases registered by month
- 4. View data queries
- 5. View form completion status
- 6. Go to relative sheets
- 7. Create or view appointments
- 8. Claim funding for Visits 8 and 9
- 9. Create participant login sheet

Submit
Data Entry

Continue to enter data, then click Submit

ID
--- please select an answer ---

Sex
Please select: Male

Date of birth
The sex and DOB fields have been added as an extra check. This information should be in the CRF under Registration. (Enter all dates as DD/MM/YYYY)

Visit date

Case visit
First make your selection above

---

Data Entry

Continue to enter data, then click Submit

ID

Sex
Female

Date of birth
02/11/1949

Visit date

Case visit
Diagnosis less than 3y V6 (30 months)

Form to fill in
1a. Medication
**ID Checker**

Please check the subject ID below.

**Registration data previously entered for this case**

<table>
<thead>
<tr>
<th>Centre</th>
<th>ID</th>
<th>Date of birth</th>
<th>Sex</th>
<th>Date of registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>APUX</td>
<td>27/04/1946</td>
<td>Male</td>
<td>10/02/2012</td>
</tr>
</tbody>
</table>

**Current data entry (from previous page)**

<table>
<thead>
<tr>
<th>Centre</th>
<th>ID</th>
<th>Date of birth</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>APUX</td>
<td>02/11/1949</td>
<td>Female</td>
</tr>
</tbody>
</table>

*Please confirm these 4 data items match*  
*Please DO NOT SELECT "YES" if these items do not match!*  
*This is an ESSENTIAL CHECK that you are entering the data for the CORRECT CASE. If the items do not match, either go back and correct them, or explain in the memo box below.*

---

**Tracking Parkinson's**

---

**Medication**

Enter data and then click Submit.

<table>
<thead>
<tr>
<th>ID</th>
<th>Centre</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>APUX</td>
<td>11</td>
<td>07/12/2016</td>
</tr>
</tbody>
</table>

Current Drugs: Antiparkinson drugs  
Select Yes for any drug class currently used

**L-dopa (including Stalevo)**

When was L-dopa first started?

**Amantadine**

When was Amantadine first started?

**Anticholinergic**

When was an Anticholinergic first started?

*Data entry forms are all unchanged*
Drug 10
Drug 11
Drug 12
Memo
any general note or reminder relating to this case or form

Is this form complete for this visit?*

Yes
Partial
No
Enter yes if all fields answered,
Partial if some fields answered (you can add the rest later),
No if none of the fields have been answered

Enter next form in sequence?

1. Yes - Diagnostic Features

Linkage to sequence of forms is all the same as before

Submit

Clinicians

Blood sample posting over Xmas 2016: Please do not post samples after December 16th

This section is for Clinical Study Centres.
It is used to review and enter data at each site.
After logging in (use your ClinBase details) you can access the same functions as before.

Make entries below, then click Submit

Email* [donaldgrosset@gmail.com]

Choose an option from the list

1. Enter data for a case
2. View or edit data for a case
3. Overview - cases registered by month
4. View data queries
5. View form completion status
6. Go to relative sheets
7. Create or view appointments
8. Claim funding for Visits 8 and 9
9. Create participant login sheet

Submit
Summary – New Web Interface

- **clinbase.co.uk** is being phased out
- All data entry, review, queries etc. are now on **trackingparkinsons.org.uk**

- There are some new features for study participants *(and resulting new features for research nurses)*....
Tracking Parkinson’s (PRoBaND) 

Direct data entry by participants 

and some other enhancements

Donald Grosset 
Consultant Neurologist and Honorary Professor

December 2016

Increasing Direct Data Entry

• Reduced protocol violations
• Reduced data entry (transcription) errors
• Major reduction in onsite monitoring
• Major time savings at clinical sites

Mitchel et al, Lessons Learned From a Direct Data Entry Phase 2 Clinical Trial Under a US Investigational New Drug Application Therapeutic Innovation and Regulatory Science 46(4):464-471 · July 2012
Layout and design improvements to our CRFs
  • these will filter through for future visits

Online direct data entry options for participants
  • definitely highly desirable
  • but not for everyone
  • don’t make a mobile phone version!
Study Participants - will launch mid-December 2016

This section is for Study Participants - Patients and Siblings

Answering the Questionnaires online is optional. You can fill them out on paper as before if you prefer.

To fill out Questionnaires you need to create your own Login (use the link below). You will need to have your own temporary password (please obtain from your local Study Nurse). After you have created your Login, you will be able fill out your Questionnaires before a Study Visit.

Create your own login

Clinicians

Blood sample posting over Xmas 2016: Please do not post samples after December 16th

This section is for Clinical Study Centres. It is used to review and enter data at each site. After logging in (use your ClinBase details) you can access the same functions as before.

Make entries below, then click Submit

Email*  
donaldgrosset@gmail.com  

Choose an option from the list

- 1. Enter data for a case
- 2. View or edit data for a case
- 3. Overview - cases registered by month
- 4. View data queries
- 5. View form completion status
- 6. Go to relative sheets
- 7. Create or view appointments
- 8. Claim funding for Visits 8 and 9
- 9. Create participant login sheet

Giving Study Participants initial login details

Use this option
You enter the Study ID as usual....

...then you see login details for the study participant, plus some guide notes

Print this sheet for the study participant

...the study participant uses this information at home
...the study participant is asked to enter some more info (we use this for data checking)

Enter your own information, then click Submit

Your Sex*  
- Male  
- Female

Your Postcode*  
G22

Your Date of Birth*  
02/02/1952

Your Email address*  
participantemail@xyz.co.uk

Now choose your own password. Make it at least 8 characters, including at least 1 number, and a mix of upper and lower case letters

Password*  
******  
- Fair

Confirm Password*  
******

Submit

...the study participant then gets a summary page

We suggest you make a note of the information below, for future use with the Study.

Once you have done this, please click Submit.

Your Study ID  
APUX

Your Centre number  
11

Your email  
participantemail@xyz.co.uk

Your postcode (first part)  
G22

Your date of birth  
02/02/1952

Your sex  
Male

Submit
We suggest you make a note of the information below, for future use with the Study.

Once you have done this, please click Submit.

<table>
<thead>
<tr>
<th>Your Study ID</th>
<th>APUX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Your Centre number</td>
<td>11</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Your email</th>
<th><a href="mailto:participantemail@xyz.co.uk">participantemail@xyz.co.uk</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>Your postcode (first part)</td>
<td>G22</td>
</tr>
<tr>
<td>Your date of birth</td>
<td>02/02/1952</td>
</tr>
<tr>
<td>Your sex</td>
<td>Male</td>
</tr>
</tbody>
</table>

...and after clicking Submit gets a confirmation message

Thank you for registering for Tracking Parkinson's online.

Please check your email - and follow the link in it - to activate your registration.

If you do not get this email, please check for it in your 'Junk' email folder.

If you still do not receive the email, please contact us (using the link on the website) and we will be happy to help.

Click here to go back to the main page of the Tracking Parkinson's website.

...then an email goes to the study participant

data@proband.org.uk
To: participantemail@xyz.co.uk
Reply-To: data@proband.org.uk
ACTIVATION required for Tracking Parkinson's

Dear Participant

Many thanks for registering to use the Tracking Parkinson's site to answer questionnaires.

Please click on the link to Activate your Registration.

http://trackingparkinsons.org.uk/activate

Following this link will fully activate the registration

We really appreciate your involvement and contribution to the Study.

Best wishes

Callum Smith

On behalf of the Tracking Parkinson's Team
<table>
<thead>
<tr>
<th>Participant Email*</th>
<th><a href="mailto:participantemail@xyz.co.uk">participantemail@xyz.co.uk</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>StudyID</td>
<td>APUX</td>
</tr>
<tr>
<td>Centre</td>
<td>11</td>
</tr>
<tr>
<td>Activate your login*</td>
<td>[✓]</td>
</tr>
</tbody>
</table>

**Update**

This validates the participant’s email

---

...the participant is now registered to use the online system for data entry

..the next steps involve the local research team...
...an email goes to the study nurse (or equivalent) at the participant’s centre

data@proband.org.uk
To: nurseresearcher@hospital.org.uk
Reply-To: data@proband.org.uk
Tracking Parkinson's Case APUX has registered for online

Dear Tracking Parkinson's colleague

The participant with Study ID APUX has registered to use the Tracking Parkinson's site for completing questionnaires.

Please go to the Tasks section of the site to see this information and the links to help you to do the following:

1. Send the participant a Welcome email.

2. Set yourself a reminder to send the participant a link when Questionnaires are due.

https://trackingparkinsons.org.uk/tasks Follow this link to see Tasks

Many thanks

The Tracking Parkinson's Team

Website Overview - Donald Grosset

Tasks

...a new registration by a study participant creates a Task for the local Research Nurse – the task is called NOTIFY

When you see a new NOTIFY task in the table below - this means that a study participant has registered for online data entry.

You should do the following 2 tasks:

1. **Send the participant a welcome email.**
   To do this, go to the Clinician page and select Messages.

2. **Mark up your own diary** to send the participant another email, shortly before they are due to come for their next visit (to alert them to fill out questionnaires).
   *Note: the system does NOT alert you to send this email, you need to mark it in your diary*

Once you have done these 2 things, please mark the task below as Completed.

<table>
<thead>
<tr>
<th>CENTRE</th>
<th>STUDYID</th>
<th>TASKNAME</th>
<th>NURSE EMAIL</th>
<th>DATE CREATED</th>
<th>COMPLETED</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>APUX</td>
<td>NOTIFY</td>
<td><a href="mailto:donaldgrosset@gmail.com">donaldgrosset@gmail.com</a></td>
<td>29/11/2016</td>
<td>No</td>
</tr>
</tbody>
</table>
System messages

Use the links below to send a message to a Study participants who has registered for online answering of questionnaires.

There are two message types.

1. Welcome message.

You will get an email when a study participant first registers to complete questionnaires online.

You should then send them are welcome email, using the link below.

Also, please note in your own diary when to send a further email, just before the study participant is due for their next visit, to advise them to complete questionnaires online. Note: there is no automatic alert for this from the website.

Link to create Welcome message

Welcome message

Please see the Messages page for more information about using this section.

<table>
<thead>
<tr>
<th>Centre</th>
<th>11</th>
</tr>
</thead>
</table>

IDs are only shown for participants who have registered for online Questionnaires

<table>
<thead>
<tr>
<th>StudyID</th>
<th>Please select then DOUBLE CHECK</th>
</tr>
</thead>
</table>

The information below is obtained from the participant’s information that they gave when creating their login. Please double-check that the Sex and Date of Birth in your records match those below.

If they do not match, do not send a message. And please advise the Glasgow Administration centre of this mismatch.

<table>
<thead>
<tr>
<th>Sex</th>
<th>First make your selection above</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Participant DOB</th>
<th>First make your selection above</th>
</tr>
</thead>
</table>
Welcome message

Please see the Messages page for more information about using this section.

**Centre** 11

IDs are only shown for participants who have registered for online Questionnaires

**StudyID** APUX

The information below is obtained from the participant's information that they gave when creating their login. Please double-check that the Sex and Date of Birth in your records match those below.

**If they do not match, do not send a message.** And please advise the Glasgow Administration centre of this mismatch.

**Sex** Male

**Participant DOB** 02/02/1952

**Date the participant registered (for online)** 02/12/2016

You can select below which email address to send the message from.

**Nurse email** Please select

---

**Tasks**

When you see a new NOTIFY task in the table below - this means that a study participant has registered for online data entry.

You should do the following 2 tasks:

1. **Send the participant a welcome email.**
   To do this, go to the Clinician page and select Messages.

2. **Mark up your own diary** to send the participant another email, shortly before they are due to come for their next visit (to alert them to fill out questionnaires).
   **Note:** the system does NOT alert you to send this email, you need to mark it in your diary

Once you have done these 2 things, please mark the task below as Completed.

.....around 2 weeks before the visit is suggested

---

<table>
<thead>
<tr>
<th>CENTRE</th>
<th>STUDYID</th>
<th>TASKNAME</th>
<th>NURSE EMAIL</th>
<th>DATE CREATED</th>
<th>COMPLETED</th>
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<td>11</td>
<td>APUX</td>
<td>NOTIFY</td>
<td><a href="mailto:donaldgrosset@gmail.com">donaldgrosset@gmail.com</a></td>
<td>29/11/2016</td>
<td>No</td>
</tr>
</tbody>
</table>
Next steps

• The participant now gets a nice email from you, with a welcome message

• ....the date for the next visit for APUX, that you have noted in your diary comes round...

• ...go to the website – find the Messages button
  - Select the case eg. APUX
  - Select the correct visit eg. V9
  - Send a message

Tracking Parkinson's

Clinicians

Blood sample posting over Xmas 2016: Please do not post samples after December 16th

This section is for Clinical Study Centres.
It is used to review and enter data at each site.
After logging in (use your ClinBase details) you can access the same functions as before.

Make entries below, then click Submit
System messages

Use the links below to send a message to a Study participants who has registered for online answering of questionnaires.

There are two message types.

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Also, please note in your own diary when to send a further email, just before the study participant is due for their next visit, to advise them to complete questionnaires online. Note: there is no automatic alert for this from the website

Link to create Welcome message

2. Visit message.

This refers to the message above, to ask study participants to complete their questionnaires before coming for their study visit.

You can check these questionnaires when they attend - to help complete any missing answers.

Link to create Visit message
Visit messages

Please see the messages page for more information about using this section.

<table>
<thead>
<tr>
<th>Centre</th>
<th>11 ♦</th>
</tr>
</thead>
<tbody>
<tr>
<td>StudyID*</td>
<td>Please select then DOUBLE CHECK ♦</td>
</tr>
</tbody>
</table>

Please MAKE SURE you select the correct study participant. DOUBLE-CHECK that the Sex and Date of Birth below match your records of the case you are sending a message to. If they do not match, DO NOT SEND A MESSAGE.

<table>
<thead>
<tr>
<th>Sex*</th>
<th>First make your selection above ♦</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOB*</td>
<td>First make your selection above ♦</td>
</tr>
</tbody>
</table>

Next Visit to alert participant about (select one)*

**Please select one**
- Diagnosis less than 3y V7 (36 months)
- Diagnosis less than 3y V9 (54 months)
- Diagnosis less than 3y V10 (72 months)
- Relative V1 Screening (0 months)
- Relative V2 (36 months)

| Nurse email (choose one)* | Please select |

Next steps

- The Study Participant gets an email with a link to completing the questionnaires

- And – about a week later – comes for the study visit

At, or just before, the visit – check if the questionnaires have been done… if not, advise participant, and ask them to do on paper
If you have already created your own login, and have lost your password, you can use the link below to reset it.

**Password recovery**

Use the link below to contact the Central Administrator about login or online questionnaire problems.

**Contact Us**

If you have already created your own login, and have lost your password, you can use the link below to reset it.

**Password recovery**

Use the link below to contact the Central Administrator about login or online questionnaire problems.

**Contact Us**

This form is for use by study participants.

Please use the form below to send a message to the Central Administrator for the study. They can help with login problems, or difficulties you have with filling out the questionnaires online.

Your initial login information, your study visit dates, and other similar items cannot be sorted by the Central Administrator. Please contact your local Study Nurse directly for such issues.
Summary

Study Participant direct data entry

• All via trackingparkinsons.org.uk and emails
• Optional and flexible
• Set-up time balanced by time saving in data entry

• Study participants
  – Are specifically directed to Q’s at correct time
  – Do not have a view and edit function
  – Have an entirely separate, personal login system
  – Are completing data direct to the main system

You can check it as soon as it is entered

All below are new features and will be shown in the Investigator Meeting (December 2016)
eCRF - View and Edit

This section links to the eCRF, for review and editing of previously submitted data.

If you want to enter data for a case for the first time, use the links from the main page instead.

If you want to use the previous layout for data View and Edit (by individual form), this is still available. (Option 2 on dropdown from main page).

In this section, you can view and edit data for an individual case, following a layout that matches the paper CRF.

First, choose the case type from the options below, which will take you to the correct Index page.

eCRF Recent Onset case

---

eCRF Index

This section is for Recent Onset cases only

To view previously submitted data for Relatives, go back to the main Clinicians page and use the drop-down system (option 2. view or edit data for a case).

<table>
<thead>
<tr>
<th>Centre</th>
<th>11</th>
</tr>
</thead>
</table>

Select an ID*

Select a section of the CRF*

- Visit 0 (Screening) Registration
- Visit 0 (Screening) Medication
- Visit 0 (Screening) BPW
- Visit 0 (Screening) PMH FH Demographics
- Visit 1 (0 months) UPDRS Clinician
- Visit 1 (0 months) Diagnostic factors
- Visit 1 (0 months) MoCA
- Visit 1 (0 months) Scans
- Visit 1 (0 months) Blood tests
- Visit 1 (0 months) PDQ to HADS
- Visit 1 (0 months) QUIP to UPDRS
- Visit 1 (0 months) NMSS PDSS
- Visit 2 (6 months) Medication
- Visit 2 (6 months) CISLIRD
eCRF Index

This section is for Recent Onset cases only

To view previously submitted data for Relatives, go back to the main Clinicians page and use the drop-down system (option 2. view or edit data for a case).

<table>
<thead>
<tr>
<th>Centre</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>APUX</td>
<td></td>
</tr>
</tbody>
</table>

Select a section of the CRF:
- Visit 0 (Screening) Registration
- Visit 0 (Screening) Medication
- Visit 0 (Screening) BPW
- Visit 0 (Screening) PHQ FH Demographics
- Visit 1 (0 months) UPDRS Clinician
- Visit 1 (0 months) Diagnostic factors
- Visit 1 (0 months) MoCA
- Visit 1 (0 months) Scans
- Visit 1 (0 months) Blood tests
- Visit 1 (0 months) PDQ to HADS
- Visit 1 (0 months) QUIP to UPDRS
- Visit 1 (0 months) NMSS PDSS
- Visit 2 (6 months) Medication
- Visit 2 (6 months) CISTI-PD
- Visit 2 (6 months) Social history
- Visit 2 (6 months) Smell testing
- Visit 3 (12 months) Medication
- Visit 3 (12 months) Diagnostic features
- Visit 3 (12 months) BFI MERQ-P-PD
- Visit 4 (18 months) Medication
- Visit 4 (18 months) UPDRS Clinician
- Visit 4 (18 months) MoCA
- Visit 4 (18 months) Blood tests
- Visit 4 (18 months) PDQ to HADS
- Visit 4 (18 months) QUIP to UPDRS
- Visit 4 (18 months) NMSS PDSS
- Visit 5 (24 months) Medication
- Visit 5 (24 months) L-dopa challenge
- Visit 5 (24 months) CISTI-PD
- Visit 5 (24 months) Tissue bank

**eCRF - PDQ to HADS (view or edit)**

Edit data and then click Update (bottom of page)

Click here to return to the eCRF index page

Click here to return to the main page

ID: APUX

Centre: 11

Case Visit: Diagnosis less than 3y V4 (18 months)

Date: 14/08/2013

Email: angieodonnell2@gmail.com

(Parkinson's Disease Quality of Life 8 - item version)
Due to having Parkinson's Disease, how often during the last month have you...
(Select appropriate answer)
1. Had difficulty getting around in public?
   a. Never
   b. Occasionally
2. Had difficulty dressing yourself?
   a. Never
   b. Occasionally
3. Felt depressed?
   a. Occasionally
4. Felt embarrassed in public due to having Parkinson’s Disease?
   a. Never
5. Had problems with your close personal relationships?
   b. Occasionally
6. Had problems with your concentration, eg. when reading or watching TV?
   b. Occasionally
7. Felt unable to communicate with people properly?
   a. Occasionally
8. Had painful muscle cramps or spasms?
   a. Occasionally

Memo:
yany general note or reminder

Are these forms complete for this visit?
Yes

Memo:
any general note or reminder
Clinicians

Blood sample posting over Xmas 2016: Please do not post samples after December 16th

This section is for Clinical Study Centres.
It is used to review and enter data at each site.
After logging in (use your ClinBase details) you can access the same functions as before.

Make entries below, then click **Submit**

**Email**
(donaldgrosset@gmail.com)

**Choose an option from the list**
- 1. Enter data for a case
- 2. View or edit data for a case
- 3. Overview - cases registered by month
- 4. View data queries
- 5. View form completion status
- 6. Go to relative sheets
- 7. Create or view appointments
- 8. Claim funding for Visits 8 and 9
- 9. Create participant login sheet

**ClinBase - View or Edit data - All forms**

Select a form and click **Submit**

**Click here to return to main page**

**ID**
APUX

**Choose a form**
PDQ8, EQ5D, ESS, RBD and HADS

Leave as SHOW ALL to return all entries at your centre or select a case from the dropdown list

Only results for the Centre number linked to your current login are available
If you have more than one centre number, return to ClinBase and log in again with your username that is linked to the other centre

**Advanced search - click here**
### PDQ8, EQ5D, ESS, RBD and HADS

Initial dating is in date order - change the sort order of a column by clicking on the header - select View Details to view or edit a record.

Click here to run another search

Click here to return to main page

<table>
<thead>
<tr>
<th>Date</th>
<th>Centre</th>
<th>ID</th>
<th>Email</th>
<th>Form complete</th>
<th>Case visit</th>
<th>(Admin code)</th>
<th>View Details</th>
<th>Delete</th>
</tr>
</thead>
<tbody>
<tr>
<td>02/02/2012</td>
<td>11</td>
<td>APUX</td>
<td>nmalek@nhs...</td>
<td>Yes</td>
<td>Diagnosis less than 3y V1 (0 months)</td>
<td>View Details</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14/08/2013</td>
<td>11</td>
<td>APUX</td>
<td>angeladodon...</td>
<td>Yes</td>
<td>Diagnosis less than 3y V4 (18 months)</td>
<td>16:04:26</td>
<td>View Details</td>
<td></td>
</tr>
<tr>
<td>12/03/2015</td>
<td>11</td>
<td>APUX</td>
<td>tracy.murp...</td>
<td>Yes</td>
<td>Diagnosis less than 3y V7 (36 months)</td>
<td>00:35:56</td>
<td>View Details</td>
<td></td>
</tr>
<tr>
<td>29/06/2016</td>
<td>11</td>
<td>APUX</td>
<td>Elaine.Tyr...</td>
<td>Yes</td>
<td>Diagnosis less than 3y V9 (54 months)</td>
<td>14:34:00</td>
<td>View Details</td>
<td></td>
</tr>
</tbody>
</table>

Records 1-4 of 4

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### eCRF Index

This section is for Recent Onset cases only

To view previously submitted data for Relatives, go back to the main Clinicians page and use the drop-down system (option 2. view or edit data for a case).

Select an ID

Select a section of the CRF

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- Visit 0 (Screening) Medication
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- Visit 4 (18 months) QUIP to UPDRS
- Visit 4 (18 months) NMSS PDDS
- Visit 5 (24 months) Medication
- Visit 5 (24 months) L-dopa challenge
- Visit 5 (24 months) Cinski-PD
- Visit 5 (24 months) Tissue bank
Tracking Parkinson’s: Thank you

Patients, siblings, and families

Now funded to 2020
