Participant Information Sheet

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Study: Parkinson's Families Project (PFP)
Chief Investigator: Professor Huw Morris. **Principal Investigator:** Professor Huw Morris
Study Coordinator: Miriam Pollard. **Tel**: 020 8016 8174
Email: ion.pdresearch@ucl.ac.uk

Parkinson's Families Project – Part 1: Outline of the Study

1. Introduction

We would like to invite you to take part in a genetics research study – the Parkinson's Families Project (PFP). Before you decide, you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for taking the time to read this and consider participation.

2. What is the purpose of the study?

We are interested in understanding why Parkinson's happens, and in developing new treatments. We know that in some people with Parkinson's, genetic (inherited) factors are important, and this can help us to understand the disease. It is rare for many people in a family to be affected by Parkinson's. The condition is passed from one generation to the next in less than 5% of cases. We hope that identifying inherited variants (in genes) that cause Parkinson's in some people will help us to understand more about the condition. As families share a common genetic background, it is much easier to find new Parkinson's genes by studying the genetic makeup of people with Parkinson's alongside other members of their families. It is useful to be able to study other family members with and without Parkinson's.

We are particularly interested in studying the genetic make-up of people with Parkinson's who developed Parkinson's on or before the age of 45, or who have a family history of other relatives affected by Parkinson's.

We are asking if you and other relatives might be prepared to join our study by agreeing to donate a blood sample (or alternatively if there are difficulties with the blood sample a saliva sample can be used), so that we can study your genetic make-up.

We will work collaboratively with other groups around the world to develop new tests for Parkinson's. We hope that ultimately this research will lead to new research avenues that mean we can develop treatments that potentially could slow, stop or prevent Parkinson's.

3. Why have I been asked to take part?

You have been invited to take part in this study because you are affected by Parkinson's and developed Parkinson's on or before the age of 45; or have another family member affected by Parkinson's disease; or carry a known gene mutation for Parkinson's.

4. Do I have to take part?

No - it is up to you to decide whether or not to take part. We have provided you with information in this sheet, which will enable you to make a decision. We are also very happy to discuss this further either in person or over the phone if you still have questions or concerns. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not have an effect on any medical care that you will receive in the future.

5. Who can I contact about the study?

Ms Miriam Pollard, Study Coordinator
Phone: 020 8016 8174
Address: UCL Institute of Neurology, Department of Clinical Neurosciences, Upper 3rd Floor, Royal Free Hospital, Rowland Hill Street, London NW3 2PF
Email: ion.pdresearch@ucl.ac.uk

Prof. Huw Morris, Chief Investigator
Phone: 020 8016 8146
Address: UCL Institute of Neurology, Department of Clinical Neurosciences, Upper 3rd Floor, Royal Free Hospital, Rowland Hill Street, London NW3 2PF

For independent advice about participating in research:

Patient Advice and Liaison Service (PALS)
Phone: 020 7472 6446/6447; (020 7472 6445 - 24 hour answer phone)
Address: Main reception, Royal Free Hospital, Pond Street, London NW3 2QG
Email: rf.pals@nhs.net

Parkinson's Families Project – Part 2: Further Information on the Study

1. How can I participate?
We will ask you to read this information sheet and then for your permission (consent) to review your clinical notes. We will ask you to complete study questionnaires about your symptoms, family history and environmental background. Completion of the consent form and study questionnaires can be done on paper or from home using a highly secure, encrypted web connection. Some of the questions may be about problems that do not affect you. We will ask you about your ethnicity. We know that some specific genetic factors are more common in some ethnic groups and in the future, these may lead to trials of new treatments. We may also ask you some questions about your symptoms and previous medical tests. We may ask you to complete brief clinical examinations of your cognition, movement and balance. We will ask for your permission to take, store and analyse a blood sample for genetic analysis. The blood sample collection should take no longer than 10 minutes. We can use a saliva sample if this is more convenient for you, which can be sent in the post. We will also ask if you are happy to be informed about future studies.

You can take as much time as you need to decide whether you would like to participate in the study. If you decide to take part, all the study procedures described above can take place in a single visit lasting approximately 1 hour. If you are participating remotely, we will ask you to complete the study questionnaires in your own time before sending them back to us.

We would also like to collect some follow-up information about your symptoms and daily living in the future. We will contact you approximately 1.5 years after you have joined in the study and approximately every 1.5 years following. We will ask you to complete some follow-up questionnaires. You can do these at home and return them by post, or by a secure online survey with encrypted connection, or by phone interview with a researcher. You will not need to come in for another visit.

In some situations we may need to contact you to obtain further information or clarification about your symptoms, clinical history or family history. We will ask for your permission to be contacted in the future, both for follow-up of this particular study as well as information about future studies. You can choose not to be contacted in the future if you wish.

With your consent, we will also share your name, postcode, date of birth and NHS number with NHS Digital. The information we share will be used by NHS Digital and other central UK NHS bodies in order to provide us with information about your health status.

2. How can my family members participate?
We will not directly contact any of your family members unless you ask us to. We would like you to ask them if they might be happy to join in the study in exactly the same way as outlined above.

3. How will my participation be kept confidential?
We will code your sample, so that a number rather than a name is used in further analysis. The link between the code and your name will be kept confidential, and your personal contact details and identifiable medical details will be kept secure on a highly secure database. We will share some of your personal details with NHS Digital and receive health status data back from NHS Digital, through encrypted secure communication. Coded samples and data (i.e. without your name) may be shared with other research groups around the world for analyses. We will store the study results centrally on a separate, highly secure web-based database. This will enable us to analyse the information gathered for this research. When this study is completed we will continue to hold the data on our computer network. You may ask for your personal information to be removed from the databases at any time, in accordance with the Data Protection Act 2018 and the General Data Protection Regulation (GDPR).

4. How will samples be taken?
We will take a blood sample of about 40ml (approximately 3 tablespoons) of blood from a vein in your arm. This is a standard procedure, which takes place in hospitals every day. There may be some minor discomfort, and there is a very small risk of bruising or a local infection, which can be treated. Sample collection can be carried out either at your local study centre, or in some cases by your local GP/practice

nurse. Donating a saliva sample involves producing saliva and collecting it in a special tube. We can send you a saliva sample kit with which you can perform the collection at home and return in the post.

5. What will happen to my sample after that?
We will extract inherited material (DNA and RNA) from the blood sample. We would also like to store white blood cells, which can be converted into a cell line to provide an ongoing DNA source at a European centre in Salisbury, Wiltshire (European Collection of Cell Cultures – ECACC). The cell line can also be used for other types of research into gene function (looking at cell chemistry). The sample will be treated as a gift for research. If this leads to new blood tests or treatments, you will not receive any compensation. The research team will work in partnership with others in the public and the private sector (e.g. pharmaceutical companies) to try to develop new discoveries for the benefit of patients. The samples will be used for research, stored and used in ongoing and future projects with the same study aims, by Prof. Huw Morris, the research team and collaborating researchers around the world.

6. What is ECACC?
The ECACC Cell and DNA Bank collects, stores, and distributes cell lines and DNA samples from people with many kinds of disorders, from family members, and from other healthy people. The purpose of this is to make specimens available for use in research, teaching, therapeutics and diagnostic purposes to responsible investigators in the UK and around the world. ECACC will take measures to protect your privacy: your blood or tissue specimen will be given a code number, and your name will not be submitted to the ECACC. Some patient identification, such as age (year of birth), sex and diagnosis, will be made available.

7. How will the analysis work?
Analysis of inherited material (DNA, RNA, Genes) will be used to determine genetic variants that might cause or increase the risk of Parkinson's and other neurological conditions. In addition, the analysis will also be used to examine genetic variants which may influence risk factors, clinical symptoms, disease progression and treatment response. Studies will be performed by the main research team and samples may be shared on an anonymous collaborative basis with other investigators working on these diseases at different sites in the UK and abroad, and this may include commercial companies.

8. Why am I being asked about sharing my personal data with NHS Digital?
Although we are collecting a lot of information through questionnaires it is also important to be able to track NHS based assessments, diagnoses and treatments. For example, it may improve our understanding of these conditions to look at diagnosis and treatment of high blood pressure in patients with these conditions or to look at factors which lead to delay in diagnosis. We will therefore ask for your permission to review your medical records which might be requested from your GP, hospital doctor or other central NHS sources, including mortality status records managed by NHS Digital. To understand disease variation this will include linking our study information with mortality status records held by the Office of National Statistics (ONS). To track the mortality status of those recruited into the study, we are asking for your permission to share your personal information (NHS number, name, date of birth and postcode) with NHS Digital for the purpose of receiving mortality data (date and cause of death) from the ONS. We will store this information on the NHS network which regularly holds personal information and on a highly secure database meeting the highest standards (Information Governance Toolkit guidelines and ISO27001 certification).

9. Can I receive the direct results of my genetic analysis for Parkinson's disease?
No, work in this study will be performed on a research basis and we are not generating clinical results for you or for your medical records. Any possible new research findings need to be confirmed before they can be used as NHS tests.

This work will progress through several stages. The first stage is to identify any possible new gene changes, which could cause disease. The next stage is to confirm these findings as accurately as possible. Then we may be in a position to advise you about new NHS genetic tests, which may be useful in accurately diagnosing the disease you have and in determining the risk of disease to other members of your family.

In some circumstances the research tests may indicate that future or existing NHS based genetic or chemical testing may be useful in accurately diagnosing the condition you have and in determining the risk of other members of your family getting the condition. **You can choose whether you wish to be informed about this in advance.** If you do chose to be informed of relevant test development we will arrange for you to be given appropriate genetic advice and this may involve a new blood test. This will be discussed with you by your doctor, a member of the clinical team who arranged the original research blood sample, or by Prof. Huw Morris and/or his team. Currently these types of tests do not lead to any new treatments or change in your current treatment, although this may change in the coming years.

We think that Parkinson's is a diverse disease and that there are different forms of Parkinson's that may respond to different treatments. At the moment there are no specific treatments for different genetic or biochemical forms of Parkinson's, but this may change in the future, and this is the primary aim of our research.

You can agree to be recontacted in the future because your genetic results, generated in this study, mean that you are eligible for a new research study. This may involve further confirmatory research or NHS tests, under a new research protocol.

You can also agree to be recontacted in the future because your genetic results, generated in our study, mean that you may be eligible or suitable for a treatment which would be prescribed by your specialist. This may involve further confirmatory clinical/NHS tests.

You would be under no obligation to take part in future studies or take specific treatment without your consent and agreement but if possible we would like to inform research participants of the development of new therapies in the future that may be helpful for them.

10. What if you identify a risk factor for another disease unrelated to the original research ("incidental findings")?

We will not carry out a comprehensive screen for variation related to all human diseases, but currently large-scale analysis means that a lot of genetic variation may be documented in your samples. The tests in this study are performed on a research basis and cannot be used for clinical care. However, if we come across something that we think may possibly have an impact on your future health or that of your family, and for which there are specific treatments or preventative measures which will help you or your family, we would like to tell you about this. For example, some forms of heart disease (such as heart rhythm problems) can be determined with a genetic test which may lead to treatment which will prevent further problems. Similarly, some cancers such as breast cancer can be associated with gene changes. If these were identified then you or other family members may be advised to have detailed screening to try and identify cancer early. If you have specific concerns about any family health issues we would recommend that you discuss this directly with your doctor. However, sometimes we identify these types of changes on an incidental basis. **You can choose whether you wish to be informed about this, in advance.** If you do chose to be informed we will make sure that you have the appropriate guidance and counseling and this will involve a repeat DNA blood test.

11. What will happen to the results of the study?

We plan to publish any results in scientific journals. Your name nor any other identifiable information would not be mentioned in any publication. We will make regular reports to funding bodies and to patient groups.

12. What will happen to the information?

We will collect and hold personal data and research data.

Personal data: We will hold written records linking participants' study codes with personal identifiable information which will be stored securely in locked filing cabinets, and on a highly secure database meeting the highest standards (Information Governance Toolkit guidelines and ISO27001 certification). We need to store your name and contact details so that we can monitor your future health and care.

Research data: Research study data will be entered and analysed anonymously using study codes. Data security will be managed within local standard operating procedures. This anonymized research data will be hosted centrally through a separate, secure web based database holding research data **without personal details**. Access to the central database will be protected and restricted to members of the

research team. You may provide consent and complete study questionnaires from home using a highly secure, encrypted web connection, although these can be completed in hand written, paper format.
Collaboration: Anonymous study information may made available to collaborators at other sites in the UK and overseas and may be made publicly available to bona fide researchers to enable the combined analysis of samples from different, large patient series around the world. This may include commercial companies. These are rare conditions and it is likely that sharing and collaboration between research groups and companies in different countries will be needed to make the best use of the study. Transfer of study data will be managed in a highly secure and anonymised format**.**

13. Who will manage the information?

UCL is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. UCL will keep identifiable information about you for 20 years after the study has finished. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information at www.parkinsonsfamiliesprojects.com or by contacting

Ms Miriam Pollard, Study Coordinator
Phone: 020 8016 8174
Email: ion.pdresearch@ucl.ac.uk

Prof Huw Morris, Chief Investigator
Email: h.morris@ucl.ac.uk

UCL will collect information about you for this research study from the local NHS site at which you joined the study, your local GP and NHS Digital. This information will include your name, date of birth, NHS number, contact details and health information, which is regarded as a special category of information. We will use this information to link to your genetic information, so we can study how genes may influence Parkinson's risk, symptoms or progression.

13. How can I find out about the progress of the research project?
We will plan to send out a regular research newsletter during the study. When the study is completed, any published findings will be shared with the participants and we will invite you to an event where the research will be discussed. We will also publicise the progress and results of research with Parkinson's UK and on our study website www.parkinsonsfamiliesprojects.com.

14. What happens if I choose not to participate or want to withdraw from the study?
Participation in the study is voluntary and you can chose to withdraw your participation at any time. If you decide not to take part or to withdraw, your current or future treatment will not be affected in any way. If you decide to leave the study (not participate in any further assessments) we will retain your data and samples for further use as described in this patient information sheet. If you request that your samples and data are removed from the study we will endeavour to destroy samples and data that you have provided but in some cases this may not be possible, e.g. when further analyses have been carried out by collaborators. If you decide to leave the study, please contact a member of the study team (contact details below) and identify, in writing or verbally, whether you would prefer your data and samples collected to be retained for research purposes or destroyed.

Ms Miriam Pollard, Study Coordinator
Phone: 020 8016 8174
Email: ion.pdresearch@ucl.ac.uk

15. What will happen if I become unable to participate after I have joined the study?
We may contact you again in the future to find out more about your condition. If in the future you become unwell and lose the ability to understand or communicate your wishes about the study we will continue to hold and study your samples but would not plan to carry out any further research procedures.

16. What are the benefits of participating?
We may learn more about your condition. We cannot promise that the study will help you but the information we get might help to treat people with similar conditions better in the future.

17. Who is organising and funding the research?
This research has been funded by the Medical Research Council and Parkinson's UK.

18. Who has reviewed the study?
The study has been scientifically reviewed and approved by the Medical Research Council and ethically reviewed and approved by REC Camden & Islington. The study is also registered on the public database ClinicalTrials.gov and on the NIHR Clinical Research Network Portfolio.

19. What if there is a problem?
If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff you may have experienced due to your participation in the research, National Health Service or UCL complaints mechanisms are available to you. Please ask your research doctor if you would like more information on this.

In the unlikely event that you are harmed by taking part in this study, compensation may be available.

If you suspect that the harm is the result of the Sponsor's (University College London) or the hospital's negligence then you may be able to claim compensation. After discussing with your research doctor, please make the claim in writing to the Professor Huw Morris who is the Chief Investigator for the research and is based at the Royal Free Hospital. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

Parkinson's Families Project – Part 3: Further information on Parkinson's Genetics

1. How can genetic variation contribute to Parkinson's?
Genes are the basic units of inheritance and we all carry genetic variation, which determine physical differences between people, for example in eye or hair colour, and height. We have similar genetic variants to our immediate family. Around 5% of Parkinson's patients have a strong genetic contribution to the development of the illness, and this may be indicated by a strong family history or an early age at onset.

2. How does inheritance of genes work in families?
There are two common forms of inheritance: dominant and recessive. We each have two copies of each gene, one from our mother and one from our father. In dominant inheritance a single gene variation (a "spelling mistake" in a gene) is passed from generation to generation and children each have a 1:2 chance of inheriting the variant. This does not always lead to disease. In recessive inheritance the risk relates to carrying two gene variants and typically there is an increased risk to brothers and sisters but not to children or parents. Recessive inheritance seems to be more important in early onset Parkinson's, occurring in people before the age of 40.

3. What is the risk to other family members of developing Parkinson's?
Usually Parkinson's is not an inherited condition. It is rare for people with Parkinson's to have affected children. Even in families where we know that there is a genetic cause, not everyone who inherits the gene variant will develop the disease. The most accurate advice depends on your personal and family history and on the results of any NHS tests that you may have done. If this is something that you or your family are worried about we would recommend that you discuss this with an NHS genetic counsellor and we can arrange for this by liaising with your local consultant and family doctor.

4. What have you discovered so far?
We have identified a series of gene variants that can cause Parkinson's. This information has been used to develop new disease models – that have helped us to better understand the disease process. We have been able to develop new NHS genetic tests. We hope in the future this will lead to new treatments.

5. Why is it important to continue investigating genes in Parkinson's?
Discovering genes that cause diseases is the start of a journey, which we hope will end with better treatment. The benefits could include the development of more accurate tests to obtain a more rapid diagnosis. This is important both for selecting the best care and possible treatment, but also to provide accurate information to the wider family about risks to other individuals. Secondly, once the gene causing a disease can be identified, the search for better treatments can start. For several rare diseases new treatments have already dramatically improved care, giving hope that this will extend to many more in the future.

6. Why are other family members important in the research process?
Each of us carries thousands of rare genetic variants, which have no effect. In individuals with disease this can make it very challenging to work out which variants could be causing or contributing to the risk of disease. The most efficient way to do this is to compare genetic makeup within families as this allows us to screen out the large number of "benign' genetic variants.