People with Parkinson's
Participant Information Sheet
PD Frontline (part of RAPSODI)

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Study: RAPSODI GD (Remote assessment of Parkinsonism supporting ongoing development of interventions in Gaucher disease)
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Introduction

We would like to invite you to take part in a research study. This is an information sheet which you should read before making a decision on participating in the study. Should you have any further questions please email the research team at pdfrontline@ucl.ac.uk or make a request for somebody to call you at a convenient time.

PD Frontline, part of the RAPSODI study

You have been given this information sheet because you have Parkinson's disease and we would like to offer you the opportunity to participate in a study which we hope will enhance our understanding of the disease. PD Frontline is a part of a larger study called RAPSODI.

The aim of PD Frontline is to build a database of participants who carry genes which are known to be associated with Parkinson's disease. In the case of those like yourself who have already developed Parkinson's disease, the rationale for this is twofold. On the one hand we would like to offer research opportunities to those who carry these genes. This means trials of drugs designed to slow down Parkinson's disease which are designed to target these genes, or studies which help us better understand which patients will respond to

these drugs. We will also try to discover new genetic variants that may affect the risk, clinical course or response to treatment in Parkinson's. We hope that this will help us to design new treatments in the future.

The RAPSODI study

If you are found to have genetic abnormality that predisposes to Parkinson's disease, we may ask you to participate in the main RAPSODI study. This would mean signing a separate consent form and undertaking yearly assessments by post and on the internet. If you choose to participate in RAPSODI, we may ask to contact your spouse/partner and blood relatives who do not have Parkinson's disease to offer them the opportunity to have genetic tests done for these genes. This would only be done with your express permission and only if we were to discover you carried one of these genes.

We wish to do this because we hope to monitor carriers of these genes over a long period of time to see if there is any evidence of the development of the earliest signs of Parkinson's disease. Ultimately our intention is, in people with a slightly increased risk of developing Parkinson's, to be able to give the same neuroprotective drugs when there is evidence that they are in the earliest stages or Parkinson's disease, to slow down or stop its progression.

Part 1 of this information sheet will explain the purpose of the study and our research into Parkinson's, the GBA gene and the LRRK2 gene.

Part 2 gives you more detailed information about the process of the study and a brief description of what taking part involves for you and potentially other family members.

Part 1.

Why do we want to diagnose Parkinson's disease earlier?

One reason we don't yet have a cure for Parkinson's disease is because the movement symptoms of the condition only appear when 50% of the nerve cells have already been lost.

We believe the nerve cells begin to be affected many years before symptoms appear, but we don't know enough yet about these early stages.

If we could identify people at risk earlier – before the movement symptoms appear – we would be in the best possible position to slow, stop or even reverse Parkinson's disease.

How could we identify people at risk of Parkinson's disease before the symptoms appear?

Ongoing research suggests that some symptoms may occur several years before the movement problems of Parkinson's disease appear.

Many older people probably experience some of these problems at some stage. But finding people who experience several of these issues together may help us identify those at a higher risk of Parkinson's disease.

How is Parkinson's disease related to the GBA gene?

In the 1990s doctors noticed that a larger number of family members of patients with a rare genetic disorder called Gaucher disease were developing Parkinson's disease than would normally be expected. These family members were found to be carriers of the glucocerebrosidase (GBA) gene. Research has since established that both individuals affected by Gaucher disease (carrying two copies of the GBA gene) and those who carry

one copy of this gene have around a 10% chance of developing Parkinson's disease by the age of 80.

Between 2-10% of patients with Parkinson's within the general population carry a copy of the GBA gene, and this figure may be even higher amongst certain groups, for example within the Ashkenazi Jewish community. This makes carrying the GBA gene the most significant genetic risk factor for Parkinson's disease, across the whole population. At present there is no effective treatment for Parkinson's disease caused by the GBA gene. The aim of this research is to discover more about the disease course of Parkinson's in carriers of the GBA gene, so in the future we can develop, test and give effective treatments as early as possible.

How is Parkinson's disease related to the LRRK2 gene?

The link between LRRK2 and Parkinson's was first described in 2002, and LRRK2 mutations are believed to be a major cause to inherited and sporadic PD.

For people from certain ethnic backgrounds, such as Ashkenazi Jewish, North African Berbers and Basque, LRRK2 mutations account for a much higher number of Parkinson's cases than that of the general population. The most widely found mutation (G2019S), is thought to account for 15-20% of cases in Ashkenazi Jews.

Although the LRRK2 gene is very rare (less than 1% of those in the Ashkenazi community and less than 0.01% of the general UK population) those who possess the LRRK2 gene have a 40% chance of developing Parkinson's by the age of 80.

By identifying LRRK2 carriers in the Parkinson's population, we will be better able to understand the relationship between mutations in this gene and the potential development of Parkinson's, and therefore develop and test the efficacy of new treatments.

Part 2

About RAPSODI GD

What is the RAPSODI project?

RAPSODI is a study designed to identify those who carry the GBA gene. Currently there are a number of potential treatments in development to stop the early loss of these nerve cells within the brain and so prevent the disease developing. These treatments are targeted at specific genetic mutations known to be associated with Parkinson's disease such as GBA and LRRK2. To test whether these treatments work will require the participation of many patients in the earliest stages of developing Parkinson's disease, as well as those with established Parkinson's disease. The end objective of the study is to provide information which will allow the identification of those carriers of the GBA gene and LRRK2 gene with early signs of Parkinson's disease, so when a potential drug to treat Parkinson's disease associated with the GBA or LRRK2 genes becomes available, we will be able to test its effectiveness on this group.

PD Frontline, part of the RAPSODI study:

Additionally, the study will identify those with established Parkinson's disease who carry a GBA or LRRK2 mutation for clinical trials of drugs which are designed to slow down Parkinson's disease within these patients. Furthermore, we believe that any treatment for Parkinson's caused by the GBA or LRRK2 gene may also be able to treat Parkinson's disease in general (i.e. in those who do not carry a genetic mutation but have been diagnosed with Parkinson's).

What will being in the study involve?

- For the first stage of the study, we will analyse your data and if eligible will ask you to provide a blood sample or should you not wish to, a saliva sample. Your sample will be collected remotely via a sample collection kit in the post. The blood collection kit attaches to your upper arm to collect your blood and does not require you to use a manual lancet – this method has been tested and found virtually painless. Blood samples provide higher quality results and are the preferential sample for genotyping, though should you for any reason feel more comfortable with a saliva sample we can provide a saliva collection kit as an alternative. More information about the blood collection kit is available later in this PIS and on our website (www.pdfrontline.com). We will then use this for genotyping purposes, to identify whether you are a carrier of a mutation in the GBA or LRRK2 gene. For those not eligible for a sample, you may remain on the study to help us with other research, and you may be contacted in the future to provide a sample.

- Once we have obtained your genetic results, we will inform you as to whether or not you are a carrier of a mutation in the GBA or LRRK2 gene. In order to participate in this first stage of the study you will need to agree to be informed of your genetic results so that we may be able to refer you to clinical trials and other studies. Carrying a genetic variant in a known Parkinson's gene (at the moment we are focussing on LRRK2 and GBA) will indicate that there is an increased risk of developing Parkinson's in your family members, but also that they may be eligible to be involved in preventative research studies. Currently, there is a 10% risk of developing Parkinson's disease associated with carrying a GBA variant by the age of 80. There is an estimated 40% risk of developing Parkinson's in those who possess a LRRK2 variant. Your sample will be stored for future genetic research as outlined below.

- If you are found to be a carrier of a mutation in one of these genes, a trained member of the study team will contact you to discuss the results and allow you time to ask any questions. You will also receive a report detailing information about the mutation. If you consent, a copy will be sent to your clinician, GP and referring NHS team. Reports for participants found to be a carrier and not found to be a carrier will be available via your account on the study portal.

- We may also need your consent to pass your contact details and some information about your genetic results and Parkinson's diagnosis onto NHS sites that are carrying out clinical trials, you can choose whether you would be happy for your details to be passed on for relevant clinical trials when consenting to the study. Please think carefully about these factors when deciding whether or not to take part and choosing your consent preferences.

- If you are found to be a carrier of a mutation in the LRRK2 or GBA gene, we shall contact you and ask permission to contact your relatives to see whether you and they would be prepared to participate in the RAPSODI study. We shall not contact any relatives without your express permission. If this occurs, on a yearly basis we shall ask you to carry out a series of internet-based assessments which include tests looking at sleep patterns, memory, mood and symptoms of Parkinson's disease. We shall also send you a postal test to assess how good your sense of smell is. We may ask some participants to provide additional samples of blood, urine and spinal fluid; this will be completely optional.

What's new about the RAPSODI project?

RAPSODI is innovative because it will be conducted almost entirely online. This means participants do not even need to leave their homes to take part, and we can process lots of information quickly, cheaply and efficiently. We hope that using the Internet will mean more people take part and potentially benefit from its results.

Taking part in RAPSODI GD

Who can take part in the study?

We are looking to recruit anyone with a diagnosis of Parkinson's to PD Frontline, the first stage of RAPSODI. For participants who are found to have a GBA or LRRK2 mutation, and who agree to continue participation in RAPSODI, we will also seek to recruit their spouses and first-degree family members (this means where possible, parents, brothers and sisters and children if over the age of 18) who currently live in the UK.

Who cannot take part in the study?

1. People diagnosed with a movement disorder other than Parkinson's disease and those with dementia or motor neurone disease.

2. Certain drugs can contribute to or cause Parkinson's disease-like symptoms. We may exclude some participants if we think their previous or current medication may affect the results of the study.

Do I have to take part in the study?

No. There is no obligation to take part in the study, and the decision to participate rests entirely with you.

You also have the right to withdraw from the study at any point and are not obliged to provide a reason.

If you do choose to participate, please read the information on these pages carefully. You will then be asked to read and complete a consent page before registering on the website.

I'd like to take part. What do I have to do?

If you would like to take part in the study, you can visit and register on our website at www.pdfrontline.com.

Will I discover whether I am a carrier of the GBA gene if I don't already know?

If you decide to participate you will be informed of your genetic status – i.e., we will inform you as to whether or not you are a carrier of a mutation in the GBA gene. If you already know that you are a carrier of a mutation in the GBA gene, we will repeat the genotyping process for the purpose of this study.
You should think carefully about this decision. Those who carry one copy of the gene have a 50% chance of passing it on to their children. If your partner also possesses one copy of the GBA gene (1% risk of the general population and 4% of the Ashkenazi Jewish community) there is 25% chance that your child may develop Gaucher disease, which in many cases is a treatable condition. There is also a 10% risk of developing Parkinson's disease associated with carrying one or two copies of the gene. Carriers of the gene may have siblings and parents who are also carriers, therefore the decision may have an impact not just on you but on others in your family. You can find more information on what the family implications of genetic testing are, and on sharing your results with your family in our website at www.pdfrontline.com. If you would like to discuss any of this we are available to talk to you about this in more detail. The study team can be contact at **pdfrontline@ucl.ac.uk** or you can phone us to discuss this on **0208 016 8413**.

Will I discover whether I am a carrier of the LRRK2 gene if I don't already know?

If you decide to participate you will also be informed as to whether or not you are a carrier of a mutation in the LRRK2 gene. If you already know that you are a carrier of a mutation in the LRRK2 gene, we will repeat the genotyping process for the purpose of this study.

You should think carefully about this decision. Those who possess the LRRK2 gene have a 40% risk of developing Parkinson's disease by the age of 80. Carriers of the gene have a 50% chance of passing it on to their children. Carriers of the gene may also have siblings and parents who are carriers, therefore the decision may have an impact not just on you but on others in your family. You can find more information on what the family implications of genetic testing are, and on sharing your results with your family in our website at www.pdfrontline.com. If you would like to discuss any of this, we are available to talk to you about this in more detail. The study team can be contact at **pdfrontline@ucl.ac.uk** or you can phone us to discuss this on **0208 016 8413**.

Will I be contacted directly by the research team when the tests are completed?

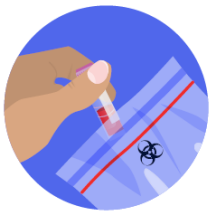
Maybe. You may also be contacted by the research team to invite you to participate in a clinical trial or study. We will only pass your information if you give permission.

Collection of and storage of biological samples

Blood and/or saliva will be collected and used to carry out genetic studies assessing Parkinson's disease risk in all patients. We will send you a collection kit in the post in order to collect this sample. You will need to send this back in the enclosed stamped and addressed envelope. This will be free of charge to return.

The blood collection kits that will be posted out are manufactured by Tasso. They attach to the upper arm and collect blood from the blood vessels in this area. They are simple and easy to use. If you would like more information about how these kits work, please visit our website (www.pdfrontline.com).

Collect patient sample.



Place sample in provided packaging.

Increasingly we are recognising that there are chemicals and compounds contained in blood and urine that may further define an individual's risk of future Parkinson's disease. For participants who are found to have a GBA or LRRK2 mutation, we may ask you to provide samples of urine, blood (additional sample) or in a few cases cerebrospinal fluid, which is the fluid from the central nervous system which is collected when we carry out a lumbar puncture. We will not ask you to do this any more frequently than once every two years.

Some samples like urine and pin prick samples of blood can be collected by yourself in your own home. Others, like some blood tests, will be taken by a nurse, doctor or research associate, either within your home or at our research sites. This will be dependent on whether your local research site has the capability to carry these out. If we ask and you agree to donate cerebrospinal fluid this will be collected by a doctor at the research site. This will involve a fine needle being inserted between the bones of the lower back.

Not wanting to give any of these additional samples will not affect your ability to participate in the rest of the study.

Taking a blood sample may cause mild pain and carries a small risk of bleeding, bruising, or infection (in less than 1% of people). Members of the research team will collect blood samples. Approximately 100ml of blood will be taken (100ml is equivalent to around 6 tablespoons). We may ask participants, by pricking their finger, to collect a very small amount of blood themselves and deposit it on a card.

Participants will be sent a pot in which to collect their own urine. 70ml (just under 5 tablespoons) of urine will be collected.

Please note, any research site/ home visits will be undertaken with robust COVID-19 policies in place, with adequate health and safety measures as dictated by government guidance and local site procedures. These apply for the duration of the current pandemic and similar public health concerns in the future.

PD Frontline may collaborate with approved national or international partners for the purpose of processing as part of genetic testing for the GBA and LRRK2 genes (Psomagen (USA), which works with the Michael J. Fox Foundation. All data and biological samples will be processed in full compliance with UK GDPR and relevant data protection legislation. Samples will remain anonymised and **your personally identifiable information will not be shared with these collaborators**. The sequencing partners will only receive the minimum necessary information to perform the analysis and all data handling will follow strict confidentiality and security protocols. Collaborators of the sequencing process are detailed on the PD Frontline website (www.pdfrontline.com).

All samples will be labelled with a unique number so as to not identify the participant. Samples will be transported to the laboratories of University College London for storage and analysis. Additional tests may be requested from external companies and institutions if required. Specifically, any samples and associated data that you provide during your participation in the study may be transferred nationally or internationally to non-commercial and commercial collaborators (e.g., National Institutes of Health (NIH) in the United States of America; Blackfynn Inc., also in the USA who work with the Michael J Fox Foundation on Parkinson's disease). Confidentiality will be maintained at all times. Information that directly identifies you, such as your name, will be replaced with a 'code' or 'ID number.' Your name and other identifying information will not be shared with other researchers. The purpose of this sample and data transfer will advance future research and the potential clinical significance of the study results through the use of more advanced analysis techniques such as artificial intelligence and whole genome sequencing.Where samples are shared with other collaborators, they may be shipped to one or more central repositories (e.g., biobank) where they will be stored and used for future research by authorised scientists and researchers.

These samples will remain shared in these repositories for the duration of our study ethics (current expiry date in 01.08.2040) and any extensions thereafter.

For a detailed outline of how your samples and data will be shared please see below.

A list of current collaborators and their scope of work is available on our website www.pdfrontline.com for you to review.

You will continue to have access to the general results of the study, including analyses of samples and data, when the analyses are reported in the medical literature. We will keep you informed of publications arising from the research.

How long will I be involved in the study?

If you are found to possess a genetic abnormality in the LRRK2 or GBA gene, we will ask you to take part in the study for up to 25 years. Although you will not be under any commitment to remain in the study for the whole duration, we hope that you will be able to make yourself available for assessments (typically an hour) every year.

Will my sample be used for future genetic research and will the data be shared?

Yes, if you agree. We have learnt a huge amount about the biology of Parkinson's through sharing anonymised samples and data with investigators from around the world. Please note that all your data will be anonymised if shared with other parties.

Your sample will be used to generate genomic data. Genes are the basic 'instruction book' for the cells that make up our bodies. Genes are made out of DNA, and all of the DNA in each cell is called the genome. Although our DNA is very similar to each other, your genomic data is entirely unique.

Your samples and data will be used to learn about the genetic differences between people with and without disease. They may also be used in additional research studies involving PD, other forms of Parkinsonism and Gaucher Disease.

These additional studies may involve development of cures, therapies and products and services for the benefit of PD and other patients.

Your sample and data are a gift for research. The future research projects may take place in universities, hospitals, non-profit groups, for-profit companies, or government laboratories.

Some of the research done with your information may one day lead to new software, tests, drugs, or other commercial products. If this happens, you will not receive any of the profits from these new products.

Where data and samples are shared with other collaborators (e.g., National Institutes of Health (NIH) in the United States of America; Blackfynn Inc., also in the USA who work with the Michael J Fox Foundation on Parkinson's disease), they may be shipped to one or more secure repositories (e.g., biobank and/or online data repository) where they will be stored and used for future research by authorised scientists and researchers. This data and samples will remain shared in these repositories for the duration of our study ethics (current expiry date in 01.08.2040) and any extensions thereafter. Prior to storage and analysis, your data and samples that were coded at our site will be labelled with a new unique code (double coded). Your name or other information that may identify you will not be attached to the stored data/ samples. Your coded data may be stored on a secured data platform. Information in this data platform can only be accessed and used by researchers who have

been granted formal approval to access data and who have signed agreements to protect the confidentiality of the information. The access agreements also require researchers to respect the laws and ethical guidelines for scientific research.

Your coded data may also be combined with data from many thousands of other people in large-scale analyses. A summary of this data may be made public (openly accessible) to anyone without restriction. Your coded data may be shared on one or more data platforms coordinated by multiple institutions that can be used by researchers around the world. These researchers may be conducting their own projects or may be working on projects coordinated by the sponsor. The data platform may be hosted on commercial cloud servers. The cloud refers to software and services that run on the Internet, instead of on a specific computer. These cloud servers meet international security and safety standards **(e.g., 128-bit data encryption) as used by online retail and online banking companies.**

You can change your mind at any time about the storage of your samples and data. You can contact our study team at pdfrontline@ucl.ac.uk and let us know that you no longer want your data/ samples stored and they will be removed and destroyed. However, in some cases, it may be impossible to locate and stop such future research on your specific data/ samples if all identifiers were stripped from your sample prior to the data/ sample being provided to other researchers or if data has already been distributed for research use.

After ethics approval for the study has expired, and no extensions have been applied, all samples will be disposed of in accordance with the Human Tissue Act 2004, and any amendments thereto, if deemed no longer useful for research. Alternatively, where samples are still deemed useful, they will be retrieved (wherever possible) and transferred to a licensed tissue bank.

A list of current collaborators and their scope of work is available on our website www.pdfrontline.com for you to review.

You will not benefit personally from sharing your data. Participating in the study may help researchers in many areas of scientific research, such as health and genetics.

Your information will be coded, which means it will not be connected to any information that directly identifies you, such as your name, address, and contact information. However, it is very difficult to make genetic information completely anonymous.

There is hypothetical risk that people that have your information could try to connect it to your identity by combining it with other personal information about you, through a process called re-identification. Also, in the future, new technologies could be developed that make it easier to connect your genetic information to your identity. The risks related to re-identification are difficult to predict at this time. Because genetic information is shared among people who are biologically related to you, it is possible that information about your family members could also be revealed. There is always a risk that information from genetic studies might be used to make certain statements or conclusions about groups or communities. In some cases, this can lead to discrimination against individuals, families, groups or communities.

Will my involvement be confidential?

Yes. All information you provide will be kept strictly confidential and will not be personally identifiable to anyone other than the study team.

Our website and all associated web applications used in this study are compliant with the international standards of data protection and data handling **(e.g., 128-bit data encryption) as used by online retail and online banking companies**.

What are the benefits in taking part?

You will receive no payment for your assistance with this study.

By taking part in this study you will be helping us find ways of diagnosing GBA or LRRK2 associated Parkinson's disease at the earliest possible stage. This could potentially pave the way to better treatments and a cure.

We envisage a viable therapeutic intervention to prevent GBA or LRRK2 associated Parkinson's disease should become available in the coming years. We believe this treatment may also be able to treat those with Parkinson's disease not caused by the GBA or LRRK2 gene. Recruitment for any clinical trial of it is likely to be drawn from participants of RAPSODI. As a study participant you may be eligible for selection in any such trial.

What are the possible risks of taking part?

There are no major anticipated risks in being part of this study. The information we collect will not be personally identifiable and will be entirely confidential.

If we ask you to donate blood or you provide blood as your genotyping sample, there is a risk of bruising at the puncture site. Those who undertake a lumbar puncture are at risk of headache as well as infection and bruising at the entry site. If we would like you to undertake a lumbar puncture these risks will be discussed in more detail at the time: you will be under no obligation to have this procedure and it will not affect your ability to participate in the rest of the study.

What happens if something goes wrong?

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 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 Prof. Tony Schapira who is the Chief Investigator for the research and is based at 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.

I am a participant of EJS ACT-PD, what can I expect?

For participants of EJS ACT-PD, PD Frontline will be carrying out the genetic testing for your sample. You will need to register for the PD Frontline study for us to manage your sample and send the genetic data on to EJS ACT-PD. Please see the collaborators page of our website and/or the EJS ACT-PD Trial website for more information about your participation in PD Frontline as an EJS ACT-PD participant.

EJS ACT-PD Website: https://ejsactpd.com/
PD Frontline Website: https://pdfrontline.com/en

How have patients and public been involved in this study?

People with Parkinson's, including carriers of the GBA and LRRK2 gene, were involved in the design and running of this study.

Who has reviewed the ethical aspects of the study?

Ethical aspects of this study have been reviewed by the London – Queen Square research ethics committee (reference number 15/LO/155)

Will my participation in the study and genetic test results be shared with anyone else?

This will be your decision. We will ask you permission to inform three groups of people involved in your care, that you have participated in the study. These are:

1) Your GP

2) The clinician who looks after your Parkinson's disease

3) The referring site (for instance an NHS hospital) that referred you

We will also ask your permission to disclose your genetic results to each of these groups.

What if I have further questions?

If you would like any further information about patterns of inheritance you can find this at:

http://www.geneticseducation.nhs.uk/mededu/modes-of-inheritance/single-gene-conditions/autosomal-recessive-conditions

Should you have any further questions and would like to request for a member of the research team to call you, please email us at pdfrontline@ucl.ac.uk

RAPSODI is in full compliance with General data protection regulations (GDPR). For more information on how we will and will not use your data please visit:

https://www.hra.nhs.uk/information-about-patients/