NHS
South London and Maudsley
NHS Foundation Trust

Institute of Psychiatry, Psychology & Neuroscience
KING'S College LONDON

Participant Information Sheet

/for participants with Major Depressive Disorder/

Gut feeling: understanding the Mechanisms underlying the antidepressant properties of Probiotics (the PROMEX study)

the PROMEX STUDY

You are invited to take part in a research study. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take as much time as you need to read the following information carefully and to discuss it with others if you wish. If there is anything that is not clear or if you would like more information, please ask the members of the research team before making a decision.

Why have I been invited to take part in this study?

You have been invited because you are currently taking an antidepressant but are still experiencing some depressive symptoms. To participate in this study, we do not want you to stop your antidepressant, but you should be on a stable dose for at least 6 weeks prior to participation and remain on this stable dose throughout the study.

What is the purpose of the study?

Recent studies have suggested that probiotics may have beneficial effects on mood, anxiety and stress. Small clinical trials in people with depression have shown that probiotics can improve depressive symptoms when taken in addition to antidepressants for as short as 8 weeks. However, it is not known how this effect occurs nor which probiotics are most beneficial. This study will aim to improve our understanding of the mechanisms underlying these effects by looking at how probiotics affect the gut, brain and the immune system in people with depression. We will also examine if changes in levels of certain bacteria in the gut correspond to changes in mood. We will do this by asking participants to either take probiotics (see the green box on the right) or placebo (a capsule with no active

What are probiotics?
Probiotics are food supplements that contain 'good' bacteria known to be beneficial for our bodies

What is the probiotic in this study?
It's a widely available probiotic called Bio-Kult Advanced that contains 14 kinds of good bacteria and comes in the form of capsules. Each capsule contains 2 billion bacteria.

Follow the link for more details about the probiotic used in this study: https://www.bio-kult.com/about-bio-kult/13-about-bio-kult-advanced

components and no therapeutic effect) for 8 weeks and comparing the differences between groups before and after treatment. Both you and the researchers will not know whether you received placebo or probiotic until the study is finished.

Do I have to take part?

Your participation is completely voluntary. You may withdraw from the study at any time without giving a reason and without any penalty or loss of benefits for your medical care. If you decide to participate in the study, we will ask you to sign a consent form to show you have agreed to take part. You will also be given a copy of this information sheet and consent form to keep. If you agree, we may also contact you for a follow up interview or invite you to take part in other similar studies. This, however, is optional and will not affect your ability to take part in the present study.

What will happen to me if I take part?

First, we will determine whether you are eligible to participate. This will be done at a screening visit (approx. 2 hours) during which a researcher will discuss this information sheet with you before you sign the consent form. Then, you will be asked questions about your depression, general health, other psychiatric conditions and your antidepressant treatments. If eligible and willing to participate, you will be asked to attend three sessions at the research site, which will take approximately 2 hours each: a baseline visit (week 1), a visit half-way through (week 4), and an end of treatment visit (week 8).

Before the baseline visit you will be randomly assigned (according to a pre-written study code) to either the probiotic or placebo group. You will not know whether you have received probiotic or placebo nor will the researchers performing your follow-up assessments.

At the baseline visit you will be given the probiotic (or placebo) capsules to take home with you. They do not need to be stored in the fridge.

You will be asked to take 4 capsules per day, 2 capsules twice a day with a meal for the next 8 weeks. Please retain and return all empty or partially full packages to us at the next study visit. You will not be given probiotics after the end of this 8 week period.

All three study visits will include the following procedures:

- Questionnaires: both you and the researcher will complete questionnaires about your mood, anxiety, quality of life, dietary intake, general health and gut health. Your weight and BMI will be measured.
- Computer task: you will be asked to complete a short computer task, in which you will be shown a series of faces and asked to identify the emotions shown.
- Blood test: at each visit a trained researcher or nurse will take a blood sample from you (approx. 25ml, or 5 teaspoons), which will be used to measure your levels of inflammation.

- Stool samples: on the day of each visit you will be asked to collect a small stool sample (the size of 2-3 blue scoops as shown in the picture below). We will use these samples to measure levels and types of bacteria in your gut. You will be provided with a collection kit (including gloves) that will contain everything you need to collect the sample in a clean and simple way that should not cause you any discomfort. You will collect the sample as part of your normal bowel movement and you can do that either at home or at the study site. The researcher will explain to you the contents of the kit and the collection instructions. You will also be given a written copy of these instructions to refer to as needed.

It is very important that the stool samples are collected correctly, so please ask the researchers if anything is unclear. There are no embarrassing questions!

Between the study visits:

A researcher will arrange to have 3 brief phone calls (15-20min) with you to check how you are doing. These will be scheduled at a convenient time for you during weeks 2 and 6 of the study, and approximately 4 months after your last study visit.

What reimbursement will I receive for taking part?

You will be reimbursed £10 for the screening visit (regardless of whether you are eligible to participate in the study or not) and £20 for each subsequent visit on a pro-rata basis, paid in one instalment after you last visit.

What are the possible benefits of taking part?

While you are not expected to benefit directly, the results of the study will help us understand better the mechanisms of depression and possibly develop new treatments in the future.

What are the possible disadvantages and risks of taking part?

Probiotics are classed as food supplements, not medication. As such, there are no significant risks or adverse effects associated with their consumption. Some people report bowel movement changes when they first start taking probiotics (e.g. diarrhoea or constipation), bloating or gas, but these effects typically normalise within a few days and do not cause significant discomfort to the majority of people. As blood samples will be taken in this study, you may experience mild discomfort or develop slight bruising, just as with any blood taking procedure.

What will happen if I don't want to carry on with the study?

You are free to withdraw at any point, without having to give a reason. Withdrawing from the study will not affect you in any way. If you withdraw from the study, we will keep the information about you that we have already obtained.

What if relevant new information becomes available?

Sometimes during a research project, new information becomes available about the compound or disease studied. Although unlikely, if this happens, a member of the team will tell you about it and discuss whether you want to continue in the study. If you decide to continue, you will be asked to sign an updated consent form.

Information about the optional neuroimaging component of this study

If eligible (see 'Risks' section below), you will be invited to take part in two optional Magnetic Resonance Imaging (MRI) sessions: one at the baseline visit and one at the week 8 visit. Each of these will take approximately 1.5hrs to complete. If you do not wish to take part in the neuroimaging sessions, you can still take part in the rest of the study. The purpose of these scans is to take images of your brain and compare activity in different regions before and after taking probiotics. You will also be given a short task to perform while in the scanner, like the computer task described above.

MRI scanning procedure: The imaging is done on a standard clinical scanning machine (example pictured on the right). There is no ionising radiation (x-rays) involved in this type of scan and if all precautions are taken, there are no known risks. For us to take pictures of your brain, you will have to lie as still as possible. The scanner consists of a powerful magnet, but you will not feel it because your body is insensitive to it.

Risks/discomforts of MRI: Because of the magnetic field, you must not have a scan if you have received metal injuries to your eyes, had metallic objects (including clips) inserted into your body during an operation, or if you have received a gunshot injury or have a heart pace maker. The radiographer will go through a list of possible risks with you before you go into the scanner, identifying with you any reasons why you should not be scanned. If you have a question about any metal objects being present in/on your body, you should inform the researcher and radiographer. The scanner itself can be quite claustrophobic; therefore, please inform us if you have a fear of enclosed spaces. As the machine can be quite noisy, headphones will be provided for adequate noise protection. There are no known long-term risks/consequences of MRI scans.

Benefits of MRI: If during the MRI scan a major abnormality that requires action is observed, you and the doctor you specify on your MRI consent form will be notified.

What will happen to any samples I give?

The stool and blood samples you give will only be used for the purposes of the study outlined above and then discarded. All samples collected from you will be labelled with your unique study number and not with any personal information. The stool samples will be transported to our partnering organisation in Norwich - Quadram Institute Bioscience, where all analyses will take place.

How your personal data will be used in compliance with General Data Protection Regulation (GDPR)

King's College London (KCL) is the lead sponsor for this study based in the United Kingdom. We will be using information from you 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. KCL will keep identifiable information about you for 10 years after the study

has finished. The legal basis for processing your personal data for research purposes under GDPR is a 'task in the public interest'. You can provide your consent for the use of your personal data in this study by completing the consent form that has been provided to you. 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 contacting KCL's Data Protection Officer Mr Albert Chan info-compliance@kcl.ac.uk or by visiting https://www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research.aspx. If you wish to lodge a complaint with the Information Commissioner's Office, please visit www.ico.org.uk.

If you are a patient of South London and Maudsley NHS FT (SLaM NHS), SLaM NHS will collect information from you and your medical records for this research study in accordance with our instructions. SLaM NHS will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from King's College London and regulatory organisations may look at your medical and research records to check the accuracy of the research study. SLaM NHS will pass these details to King's College London along with the information collected from you and your medical records. The only people in King's College London who will have access to information that identifies you will be people who need to contact you about taking part in the research or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

What will happen to the results of the research study?

The results of this study will be published in international journals, presented at conferences and form a part of an academic dissertation. You will not be identified in any report or publication.

Who is organising and funding the research?

The Sponsors of this study are KCL and SLaM NHS. The study is organised by the IoPPN and funded by the Medical Research Council (MRC) DTP iCASE studentship programme.

Who has reviewed the study?

The scientific quality of this study has been peer-reviewed as part of the MRC DTP project selection process. It has also been reviewed by the Health Research Authority and a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study was given a favourable ethical opinion for conduct in the NHS by London - Surrey Research Ethics Committee (REC reference: 19/LO/0761).

What if there is a problem or I need further information?

Dr Stone can be contacted using the details below with any problems, complaints or questions about the study. If these are not resolved or you would like to make a formal complaint, you can contact the South London and Maudsley NHS Foundation Trust's Patient Advisory Liaison Service

(PALS) on 0800 731 2864 or pals@slam.nhs.uk. If you would like further information about the study, please use the contact details below:

PROMEX study email address: PROMEXstudy@kcl.ac.uk; Viktoriya Nikolova, PhD student: viktoriya.nikolova@kcl.ac.uk;

Prof. Allan Young, Principal Investigator: allan.young@kcl.ac.uk; 020 7848 0088

Postal address: Centre for Neuroimaging Sciences, PO 89, Institute of Psychiatry, Psychology and Neuroscience, King's College London, De Crespigny Park, London SE5 8AF

Thank you for taking the time to read this information sheet and for considering taking part in the study!