The **L**ithium versus **Q**uetiapine in **D**epression (**LQD**) study

Patient Information Sheet

A RANDOMISED PRAGMATIC TRIAL COMPARING THE CLINICAL AND COST EFFECTIVENESS OF LITHIUM AND QUETIAPINE AUGMENTATION IN TREATMENT RESISTANT DEPRESSION

We would like to invite you 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 time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Part 1 tells you the purpose of this study and what will happen if you take part. Part 2 gives you more detailed information about the conduct of the study.

PART 1

What is the purpose of the study?

Many people who receive antidepressants for depression fail to respond adequately to this treatment. One recommended treatment option for people who have failed to respond fully to antidepressants includes adding an additional medication to the antidepressant. These add-on medications include lithium and quetiapine, which is a low dose atypical antipsychotic. There have been very few studies comparing these treatment approaches head to head. One short-term study (6 weeks) found quetiapine was just as effective as lithium. However, there has been no long term follow up study to determine which of these medications is more effective at treating depression and which is more cost effective over a longer time period.

This study aims to investigate which add-on therapy (lithium versus quetiapine) is more effective at reducing symptoms of depression over a 12 month period, which is more tolerable and best improves quality of life for patients. We are looking for 276 people with treatment resistant depression (those who have not adequately responded to two or more antidepressants in the current episode of depression) to take part.

Using a random process (like tossing a coin), half of the participants will be allocated to the decision to prescribe lithium and the other half, quetiapine so we can compare the effects of each therapy. The results of this research could help advise patients and clinicians which is the best add-on treatment for patients with treatment resistant depression.

Why might I be invited to take part in this study?

We are asking people to take part in the study if they:

- *are currently experiencing depression and have taken two or more antidepressants in the current episode*
- *are aged 18 or over*
- *do not have a diagnosis of bipolar disorder*
- *are not currently experiencing psychosis*
- *are not pregnant, currently breastfeeding, or a woman planning on getting pregnant in the near future*

Do I have to take part?

You can take as long as you wish to decide whether or not you want to take part. If you decide to participate in the study, we will ask you to sign a consent form to show you have agreed. You will be given a copy of this information sheet and consent form to keep. You are free to withdraw from the study at any time, without having to give a reason, and this will not affect any aspect of your normal care.

What will happen to me if I take part?

Both quetiapine and lithium (the treatments being researched in this study) are currently approved treatments that are recommended for use as add-on therapies to antidepressants in treatment resistant depression. We will provide you with detailed information leaflets about the medications. If you have not yet received these, please request a copy as it is important you are aware of how you should take these and potential side effects before deciding whether to take part in the study.

If you are interested in taking part we will arrange a time to speak to you so you can ask us questions about the study. If you do decide to take part we will then ask you to attend an assessment where you will you will first be asked to sign a consent form. This assessment session will be arranged at a time which is suitable for you and will take approximately 4 hours, which can be split over one or two visits. After signing the consent form, we will ask you to complete a variety of questionnaires about your current mood. In this session there will also be a clinical interview with a researcher and/or clinician working on the study to make sure you are eligible to take part. If you have a carer we will request your permission to ask them a few questions too, either over the phone or in person. Finally, we will also conduct a number of physical examinations including your height and weight, and an optional fasting blood sample (approximately 5 teaspoons – 25ml). This is so we can monitor any health related changes over the course of your medication. If you have an existing secondary care mental health clinician we will let your current doctor know that you are interested in taking part in the study, ask if they are happy to prescribe the medications and engage in the trial and know of no reason that you should not take lithium or quetiapine before this assessment. Otherwise you will be initially treated by a secondary care clinician who is already a member of the trial team.

We will randomly assign you to the decision to receive either lithium or quetiapine medication and let you and your clinician know which medication you have been assigned. You / they will then arrange an appointment with you so they can prescribe the medication and complete any necessary health checks to make sure you are suitable to take the medication, as they would do for anyone they prescribe these medications to. These medications will not be prescribed to you if we find any medical reasons why they would not be suitable. You will receive routine, best-practice treatment with your doctor to prescribe and monitor your medication, for example having any necessary blood tests and physical checks (please note, these blood tests are not optional unlike the additional blood tests at study visits). The study medication will be prescribed and monitored initially by a trial clinician. After this your care may be split between the trial clinician, other secondary care clinicians and primary care clinicians i.e. your GP over the course of your treatment as is standard NHS practice. These doctors will decide with you whether or not you should continue the medication.

We will call you after 4 weeks to see if you have started taking either study medication and to ask you a couple of questions about this. We will also arrange further study appointments at 8, 26 and 52 weeks after your first study appointment. These appointments will be similar to the first appointment outlined above and will involve questionnaires, a blood test (optional, approximately 5 teaspoons – 25ml) and

physical checks. These appointments will take around 3 hours and again will be arranged at a time that suits you, either in a hospital or university building. Reminders will be sent to you by a researcher before your next appointment is due. We have arranged these four (or five) visits over the course of the year as it is important to know the long term effects of prescribing these medications. You and your clinician may make the decision to stop taking lithium or quetiapine at any time and that is okay and will not affect you taking part in the study. We would like to monitor your symptoms and include you in the study regardless of whether you stop taking the medication before the end of the one year study period.

We will also ask you to fill in a few questions each week via a monitoring system called True Colours which is used in the NHS. This will allow you and researchers on the study to monitor your symptoms and medication closely over the duration of the study. Feedback suggests that many patients find this system useful for monitoring their symptoms. It is quick, easy to use, and reminders will be sent to you automatically letting you know when it is time to complete the questions. You can complete them on the internet, via SMS or on paper and we will give you training and the opportunity to practice using this system in the first visit. If you would like to receive more information about this system please contact a researcher on the study and they will be happy to send it to you.

Please note, we will reimburse your travel expenses to study visits. The visits will typically take place at either the participating university or hospital site.

What are the possible benefits of taking part?

The study medications may improve your symptoms of depression. There is the possibility that the study may not directly benefit you but if you do decide to take part, you will be helping medical research. The results of this study could help guide future clinical practice by informing us about which (if any) treatment is most effective.

What are the possible disadvantages and risks of taking part?

It is possible that you may experience unwanted side effects of the medication that you receive; we will monitor these during the trial. Please note, not everybody who takes these medications will get side effects. Many side effects go away with time, but some may last longer. Both medications have been used to treat people with mental health problems for a long time and therefore their side effects are well known. The information below lists the commonly reported side effects for both lithium and quetiapine (more information is provided in the medication booklets we will provide for you including the likely frequency of these effects, please feel free to request these now if you have not already):

Common side-effects of lithium include (occurring in approximately 1 in 10 people): upset stomach (particularly at the start of treatment), fine shake ('tremor') of the hands, metallic taste in your mouth, increased thirst and need to pass urine, feeling faint or dizzy, and weight gain.

Common side-effects of quetiapine include (occurring in approximately 1 in 10 people): headache, feeling dizzy or light-headed when standing up, weight gain, dry mouth, and feeling sleepy or drowsy.

Some of the questionnaires we will ask during the study concern personal information about your symptoms of depression. If you find any of the questions distressing, please tell a researcher. Team members (including clinicians) will be available to talk to if you wish. Please also note, you can take a break at any point in the study visits.

What happens when the research study stops?

We will keep in touch with you to let you know the results of the study if you wish. You may want to stay on the add-on medication after the study has ended. This decision will be made between you and your treating clinician.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information about this is given in Part 2 of this document. Please contact Professor Anthony Cleare (Anthony.cleare@kcl.ac.uk) if you have any complaints about the study. Or to talk to an independent body, please contact your local Patient Advice and Liaison Service (PALS). You can find your nearest PALS office on the NHS Choices website or ask your GP surgery, hospital, or phone NHS 111 for details.

Discontinuation of the study by the experimenter

At any time during the study, the sponsor and researchers have the right to terminate your participation in the study, for example, due to safety concerns.

Contact Details:

If you would like more information, or want to discuss the study with a member of the research team, please contact Rachael on: 07902774464 or e-mail: LQDstudy@kcl.ac.uk.

Information about an optional collaboration project

You will also have the *option* of consenting to provide some additional biological samples as part of our collaboration with the BioResource project for Mental and Neurological Health. This includes collecting either saliva samples or additional blood samples for genetic and inflammatory marker research(which can be taken with the other study blood tests, approximately 5 teaspoons – 25ml). You also have the option of providing hair samples as part of this collaboration. You can select whether you would like to provide all or any combination of these samples. . If you agree to this additional part of our project, we will also send a copy of your consent form and contact details to the South London and Maudsley NHS Foundation Trust BioResource so they can contact your for more information or about future research studies (this future contact is optional but if you agree to take part in this BioResource project sending your documents and samples to the BioResource is required).

What is the Bioresource Project?

It is part of national NHS project to build up a central library of information (or "BioBank)" about people's health. It will be used in scientific/medical research to help us better understand why different mental illnesses happen and how we can develop better treatments for them.

They aim to collect:

- Biological samples – blood and/or urine, hair, saliva for genetic and biochemical testing.
- Clinical data - Examinations by doctors, family information, your response to treatment etc.
- Neuroimaging data – X-rays and brain scans.

This data and the biological samples will be kept locally and at the South London and Maudsley NHS BioResource and will also be shared with the National BioResource (this is optional). In addition, samples and anonymised personal information may also be made available to other scientists working in biomedical and healthcare research that may include the participation of commercial companies. We may also invite you to take part in other research studies based of the information we collect. If

you are contacted for any follow-up studies, it is up to you to decide whether you would like to participate or not.

Clinically relevant genetic findings: You will usually not be given any individual feedback on risk for medical conditions from these analyses. The results are general for research purposes only and not for clinical diagnosis or treatment. If we do find something that is of known effect for which there are implications for treatment we will write to your GP recommending further investigation.

This completes Part 1 of the Information Sheet. If the information has interested you and you are thinking about participating, please continue to read the information in Part 2 before making a decision.

PART 2

What if relevant new information becomes available?

It is possible that whilst performing normal medical checks we may identify a significant abnormality that you didn't realise you had. If this occurs we will inform you as well as your GP and other clinicians (if applicable). You will also have the opportunity to discuss this with a trial clinician. Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. Although unlikely, if this happens, a member of the research team will tell you about it and discuss whether you want to, or should, continue in the study. If you decide to continue in the study you will be asked to sign an updated consent form. If the study is stopped for any other reason, you will be told why without your continuing care with your clinician being affected.

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

If you withdraw from the study, we will retain and continue to use any data collected before such withdrawal of consent unless you request that you do not want us to use any data collected from you.

How do I get help if I am concerned about anything?

If you have a concern about any part of this study, you should ask to speak with a study clinician or researcher who will do their best to answer your questions. You should report any adverse events or medical occurrences that you experience whilst in the study to a member of the study team. If you have any medical concerns that cannot wait until you can talk to a member of the team you should get help from your GP or secondary mental health care professional using the information in this sheet to tell them about the study. If we are concerned about you during the study, it is possible that your health professional will be contacted. We will always make an effort to ask for your approval before contacting your health professional.

If you have any questions about the study, if you want to know your rights as a research volunteer, if you want to tell us about any side effects, or if you want to make a complaint please contact us at LQDstudy@kcl.ac.uk or 07902774464.

This trial is co-sponsored by King's College London and South London and Maudsley NHS Foundation Trust. The co-sponsors will at all times maintain adequate insurance in relation to the study independently. Kings College London, through its own professional indemnity (Clinical Trials) and no fault compensation and the Trust having a duty of care to patients via NHS indemnity cover, in respect of any claims arising as a result of clinical negligence by its employees, brought by or on behalf of a study patient. Participation in this study does not affect your normal rights to complain about any aspect of your treatment and care. If you need to discuss this, freephone 0800 731 2864 or by email at pals@slam.nhs.uk. Finally, if you have private medical insurance you should consult with your insurer before agreeing to take part.

Will my taking part in this study be kept confidential?

We will tell your GP and other relevant healthcare professionals that you have agreed to take part in the study so they can record your involvement and let us know if there are any reasons you should not take either quetiapine or lithium. We'll also inform your GP/clinician if we learn of any safety concerns or health related issues they should be made aware of.

All information which is collected about you during the course of the research will be kept strictly confidential and stored securely in a locked cupboard or on appropriate servers. Only members of the clinical or research team will have access to your data. This means that no one, other than members of the research team, will be able to identify you from any of the data that you provide. Your medical records may be examined by people from the sponsor, regulatory authorities or NHS Trust to check that the study is being carried out properly. However, any information about you that leaves the hospital will have your name and address removed so that you cannot be recognised from it.

By signing the consent form you agree to this access for the current study and, with your additional permission, any further research that may be done. However, the study team will take steps to protect your personal information and will not include your name on any sponsor forms, reports, publications, or in any future disclosures, to ensure your personal data is protected. These will include not sharing any information which could potentially lead to someone learning your identity outside of the study site.

At the beginning of the study, you will be given a number that will be used to identify all information we keep about you. Your name, address and other identifiable information about you, will be kept in a separate place so that it will not be possible to identify any data stored about you. The data will be stored for a minimum of 15 years and then disposed of securely. The procedures for handling, processing, storage and destruction of the data will comply with the Data Protection Act.

What will happen to the results of the research study?

The findings will be used to improve guidelines for treating treatment resistant depression. The results of the study will be published in academic peer reviewed journals, presented at conferences and discussed at other public events. We will also produce a newsletter summarising the findings of the study which we will send to you and your clinical team. You will not be identified in any report or publication.

Who is organising and funding the research?

The study is organised by the Institute of Psychiatry, Psychology & Neuroscience, King's College London. Funding is provided by the National Institute for Health Research, Health Technology Assessment programme. The researchers involved in conducting this study do not receive any financial incentives for including you in this study and do not benefit financially from this study.

Who has reviewed the study?

This research has been notified to The Medicines and Healthcare products Regulatory Agency (MHRA) and reviewed by the Health Research Authority and an independent group of people, called 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 the East of England - Cambridge South Research Ethics Committee, application number: 16/EE/0318.

Thank you for thinking about taking part in the study. Please get in touch if you have any questions.