Participant Information Sheet

Ethics Approval - UQ HREC 2017000186 and QUT HREC 1700001111

Project Title: A randomised placebo controlled clinical trial investigating the role of a combination of probiotics and magnesium orotate for the management of depression.

Plain language project title: Probiotics as a treatment for depression

Principal Investigator: Dr Esben Strodl, Faculty of Health, Queensland University of Technology
Co-Investigator: Dr Matthew Bambling: Faculty of Medicine, University of Queensland
Co-Investigator: Professor Luis Vitetta: School of Medicine, University of Sydney
Co-Investigator: Professor Gerard Byrne: Faculty of Medicine, University of Queensland
Co-Investigator: Dr Sean Hall, Medlab Clinical Ltd, Sydney

Purpose of the study

Do you struggle with depression and would like to try a novel probiotic supplement designed for treating this condition? If so we would like to hear from you.

The University of Queensland School of Medicine and Queensland University of Technology School of Psychology and Counselling is conducting research into depression by testing a probiotic nutraceutical product. The research project will be conducted in Brisbane at the Institute of Health and Biomedical Innovation (IHBI) at the Queensland University of Technology or the University of Queensland Centre for Clinical Research (UQCCR) where you will need to visit for an intake interview if would like to participate.

What is involved?

Participants will need to be prepared to be allocated to an active or placebo condition. A participant allocated to the placebo condition will not take the probiotic formula and instead take a capsule that contains no active ingredients. Placebo capsules are safe and are plant based. However, all other aspects of participation such as duration, tests and completing measures are exactly the same as those in the active treatment condition. Participants won't know which of these 2 conditions they have been allocated. While this may be disappointing, the addition of a placebo-control group is essential for this kind of clinical research to identify the real effects of the intervention. See below for more information.

Study Criteria

Inclusion Criteria:

- Meet diagnostic criteria for depression according to a structured clinical interview
- Participant will not change the standard care that they are receiving without consulting a primary care physician regardless of clinical improvement during the study.

- Participants that present with a high degree of comorbidity on Axis I, II, III (ICD-DSM criterion) will be accepted into the study, given that complex mood, personality and health problems are common in patients diagnosed with depression.
- Eligible participants will be 18 years of age with no upper age limit.
- Participants will be asked not to be currently administering any nutritional supplements or any herbal medicines that have been shown to have antidepressant effects (a list will be provided to participants).
- Participants will be advised not to "self-medicate" with probiotic supplements or any prebiotic supplements for the duration of the trial.
- Be under the care of a medical practitioner who is aware of your depression e.g. your family doctor or a psychiatrist and provide their contact details to us as well as permission to contact them if necessary.

Exclusion Criteria:

- Participants diagnosed with co-morbid schizophrenia, depression as part of bipolar, or current substance misuse will not be eligible.
- Participants with current high suicide risk will not be eligible.
- Participants prescribed any form of antibiotics, currently or during previous 4 weeks may be considered for inclusion (if last 4 weeks, wait for entry).
- Patients currently taking Warfarin will not be eligible.
- Participants who are pregnant or planning pregnancy over 16 weeks will not be eligible.
- Serious physical illness (e.g., serious life threatening illness or palliative care)
- Participants administering medications other than SSRIs, or, SSRIs in conjunction with other antidepressants will not be eligible.
- Participants already taking probiotics under advisement of a health professional will not be eligible.
- Participants with an established or suspected obstructive/central sleep apnoea, as indicated in PSQI will not be eligible

What to expect

- This is a 16 week trial and 4 visits to either the Institute of Health and Biomedical Innovation (IHBI) at Kelvin Grove or the University of Queensland Centre for Clinical Research (UQCCR) at Herston are required. The active part of this study will be 8 weeks, at which point the intervention will end. However, you will be contacted again at 16 weeks post-enrolment for follow up paper assessments. You should be prepared to make this commitment before consenting to participate.
- You will be invited to two intake assessments. The first will take approximately 1 hour to complete. There will be a series of paper measures and a brief discussion of your history with depression, significant life events and any other general mental/physical health history. Should you chose to participate, we will also assess your heart rate using a non-invasive method that should not cause any discomfort. It involves placing three electrodes on your

wrist for a few minutes. At this assessment, we also ask you to supply a small blood sample*, which will be taken at the QML clinic across the road from IHBI. In addition, you will be given a dietary monitoring form to record what you eat in the 3 days prior to returning for your second visit. Finally, you will be provided with a fecal sample** kit to take home and return on your second visit to IHBI or UQCCR.

- At the second assessment you are supplied with either a placebo or the active product and can begin participating in the trial. We ask you to complete a daily log of medication adherence, and a weekly mental health questionnaire. At week 4 you will need to return to UQCCR or IHBI to collect more product and the second fecal sample kit. At week 8, you are asked to return to IHBI or UQCCR for a final visit. At this appointment you can provide the final blood and fecal samples, have your heart rate measured again for 5 minutes and complete paper measures. Between week 8 and 16 there are no study requirements, but we ask you to discontinue use of the product. A final follow-up assessment will be conducted at 16 weeks at either IHBI or UQCCR, you will be asked to engage in a structured clinical interview as well as complete paper measures. You can return your paper based assessments by mail (self-addressed envelopes will be supplied).
- You will be given written information on all aspects of this study regarding when to fill out your paper measures and when use the product.
- *Your dose will be 4 capsules a day divided into 2 equal doses morning and evening.* We will supply the capsules to you at your intake assessment and week 4 of the trial.
- All assessments will be booked with our research staff at either IHBI or UQCCR at a time of mutual convenience. Parking is not available at UQCCR, however there are multiple bus stops nearby. Parking is available in nearby streets surrounding IHBI at Kelvin Grove.
- You should be prepared to be allocated to either an active treatment or a placebo condition for 8 weeks.
- If you participate in the study we will contact you via phone or email once a week to monitor your progress. Participation is voluntary and you are able to end your involvement at any time during this study. Any data that has been collected from you up to this point will be retained for use in the research project
- For the initial assessment at IHBI/UQCCR you will be reimbursed $10, and for every subsequent assessment you will receive $20. Additionally, all study completers will receive a $25 voucher and one free bottle of the study product to thank you for your efforts.

* A small blood test sample (approximately 10ml) pre and post supplementation is the best way of diagnosing dysbiosis and will help in understanding any treatment effect. We will coordinate the sample collection and shipping for analysis. Your sample will have no personal identifying information and will be coded with a special number for the study. However, the researcher will retain identification of your sample until it has been processed, at which point they will de-identify your sample data.

** Likewise, fecal samples will help establish the probiotic bacteria is working and adding the required strains to the intestines. You will be provided with a sample kit to take home at your first (week 0) and

third assessment (week 4). You can return these kits to a researcher at your second (week 0) and fourth (week 8) visit to UQCCR or IHBI.

All tests are single purpose and no other testing can be done on your samples.

- Once again, this clinical research project requires a significant time commitment and there are regular forms and questionnaires we will ask you to complete. Therefore it is good to carefully consider these matters before committing to this study. While we ask for a willingness and ability to participate with the assessment protocols of the study we realise that things can change for people when participating and therefore you have the right to withdraw at any stage for any reason without penalty.

Risks

The product contains a combined special strain probiotic formula. All the probiotics are found naturally in the human body. These probiotics are believed to normalise peripheral and central nervous system feedback, improve cell function, improve communication pathways in the brain and reduce inflammation. Probiotics are very safe and have no known side effects.

While a minor procedure, the blood tests might be unpleasant or inconvenient for some people. The research staff member will be experienced in taking blood samples. Please let us know if you have difficulties with providing blood samples at intake. Likewise, providing fecal samples might be unpleasant for some people, however the home testing kits are efficient and hygienic and the addressed pre-paid packaging is suitable for immediate postage to our testing laboratory.

On occasion, completing questionnaires that assess symptoms of depression, anxiety and stress may be upsetting. Please alert research staff immediately if you become distressed during the initial intake assessment from this. We can discuss any concerns and you will be referred to your GP for further consultation.

A researcher will contact you weekly throughout the study to monitor your progress. At this time you can report any notable changes in physical or mental health. If you have a major concern about the effect of the treatment or your safety, please contact the lead investigators (Dr Bambling or Dr Strodl) immediately. It is also advised that you speak with your GP about physical health concerns.

Should you be unhappy about any aspect of your participation you are free to contact the researchers at any time.

Benefits and costs

Benefits of this research are that the assessment, supplements and all materials will be provided to you free of charge. This study will contribute to knowledge about the treatment of depression. You will have access to the findings of this study and can make a decision based on the results as to whether you wish to take the product or similar product once the study has completed.

The main cost to you will be your time. The study involves 4 visits to UQCCR or IHBI, daily use of tablets for 8 weeks, and completion of paperwork. The paperwork includes one monitoring booklet (completed daily), 8 questionnaires (completed weekly) and additional surveys (completed at weeks 1, 8 and 16). Given these requirements, it is important to consider carefully if you have the time and

interest to participate. To compensate for travel costs and your time, participants will receive $10 for their first visit, and $20 for subsequent visits to IHBI or UQCCR, and study completers will receive a $25 voucher together with a free bottle of product.

Confidentiality and data security

Your participation in this study is confidential and we do not pass your information on to anyone else other than your medical practitioner if you chose and consent. The lead researcher and research staff in this study will know your identity for the duration of the study, and then all data will be deidentified. It will then be impossible to link your name to the results to ensure your privacy.

You will be given feedback directly about your assessment. However, after the study has finished and data is non-identifiable, individual feedback will not be possible. A brief summary of the study results may be available on completion of the trial, if participants request further information. This study is being funded by Medlab, however only de-identified aggregate findings will be shared with Medlab.

You are free to withdraw from the study before completion at any time and we may use your data in a de-identified form as part of our evaluation with the data of the participants who have completed the treatment. This study is being funded by Medlab, however only de-identified aggregate findings will be shared with Medlab. Professor Vitetta has an existing relationship with Medlab and has been involved in clinical trials funded by them in the past.

This study adheres to the Guidelines of the ethical review process of The University of Queensland and the *National Statement on Ethical Conduct in Human Research*. Whilst you are free to discuss your participation in this study with project staff (contactable on 0466532314), if you would like to speak to an officer of the University not involved in the study, you may contact the Human Ethics Coordinator on 3365 3924.

Register for the trial at: **http://qut.to/c8b7r**

Contacts

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