PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Title	The efficacy of adjunctive *Garcinia mangostana* Linn. (mangosteen) pericarp for the treatment of schizophrenia
Sponsor	The University of Queensland
Coordinating Principal Investigator	Professor John McGrath
Principal Investigators	Professor John McGrath
Location	
Protocol	CADENCE-M

This Participant Information and Consent Form is 13 pages long. Please make sure that you have all of the pages.

Introduction

You are invited to take part in a multisite clinical trial (CADENCE-M) which is a collaborative study between Deakin University (in Geelong, Victoria), The University of Queensland and Queensland Health. This is because your treating psychiatrist has previously given you a diagnosis of schizophrenia or schizoaffective disorder. The clinical trial is testing a new add-on treatment for those with schizophrenia or schizoaffective disorder. Before you decide if you wish to consent to your participation we would like you to understand why the study is being done, what it will involve and how your information will be used. Please take time to read the following information carefully and if appropriate discuss it with friends, family and your doctor. One of our team will go through the information sheet with you and answer any questions you have. Please ask questions about anything that you do not understand or want to know more about.

Participation in the clinical trial is voluntary. You are free to refuse to participate without it affecting your current or future care. It is desirable that your doctor be advised of your decision to participate in this study. If you have a doctor we strongly recommend that you inform them of your participation in this study. Once you understand what the project is about and if you agree to take part in it, you will be asked to sign the Consent Form. By signing the Consent Form, you indicate that you understand the information and that you give your consent to participate in the clinical trial. You will be given a copy of the Participant Information and Consent Form to keep as a record.

What is the purpose of this study?

Psychotic disorders include groups of illnesses that may affect a person's thoughts, perceptions, emotions or communication. Persons may experience psychotic symptoms due to a problem with the brain's natural chemicals. Oxidative stress is believed to be one factor that may impact on healthy brain function. When the levels of antioxidants in the brain are decreased or the levels of oxidants (free radicals) are increased the balance is shifted and may lead to altered brain function. This is known as oxidative stress. Mangosteen pericarp may help to reduce the imbalance and damage caused by oxidative stress.

This trial aims to determine if receiving a dietary supplement in addition to your regular treatments, helps recovery. This dietary supplement is an extract from the mangosteen fruit and is called mangosteen pericarp. Mangosteen pericarp is produced from the outer rind of the mangosteen fruit and is a health supplement not yet registered with the Therapeutic Goods Administration. Mangosteen pericarp is an experimental treatment. This means that it is not an approved treatment for schizophrenia in Australia.

Your participation in this trial will help to increase our understanding of how mangosteen may help persons experiencing illnesses similar to yourself.

This research has been initiated by the Coordinating Principal Investigator, Professor John McGrath who is employed at the University of Queensland (Queensland Brain Institute). The research has been funded by the Stanley Medical Research Institute in the United States of America.

Do I have to take part in the study?

No, you do not have to take part in this clinical trial. It is voluntary. If you decide to take part you will be given this Participant Information Sheet and asked to sign the attached Consent Form. You will be given a copy to keep for your records. If you decide to participate you can change your mind at any stage without this affecting your routine treatment or future health care.

What does participation in the study involve?

You will be participating in an add-on double-blind randomised placebo-controlled trial. The word add-on for this clinical trial indicates that you can remain on your usual treatments and will take the trial medication *in addition* to your usual treatment. A placebo is a medication with no active ingredients. It looks like the real thing but is not. The term randomised indicates that you will be selected into either the mangosteen or placebo groups completely by chance (e.g. flip of a coin). This clinical trial will randomise participants in a 1:1 design, which means there is an equal chance of being in either the mangosteen or the placebo group. You will be participating in a double-blind study. This means that neither you nor the research staff will know which treatment group you are in until the very end of the entire study. However in certain circumstances the trial Doctor can find out which treatment group you are in. Continual review and oversight will take place regarding the efficiency and safety of the experimental products and this will allow early detection of any problems research participants may experience. By keeping you and the research staff unaware of which treatment you are on, and then comparing symptoms in patients on mangosteen pericarp versus placebo, we will be able to learn if mangosteen pericarp works in treating schizophrenia. This type of evidence can help all patients to receive better treatments in the future.

At the completion of all participants in the study, participants will be notified which arm of the study they took part in.

Step 1 Screening Process

At first contact with a member of the research team, you will be asked to take part in a diagnostic interview which will take about 2 hours. If this interview confirms that you meet the study inclusion rules, you will be provided with the opportunity to enter the next phase of the study.

Step 2 Medication regime

You will be asked to take two capsules once a day with food at a time that suits you. Each capsule will contain either 500 mg of mangosteen pericarp, or placebo. You will be asked to take the experimental medication for a total of 24 weeks.

Step 3 Contact

Contact with a member of the clinical trial team will be face to face visits, once a month.

At each face to face visit, a member of the clinical trial team will conduct a series of clinical assessments which will take approximately 1 hour to complete. This will involve asking questions about your mental and physical health including any side effects you may have experienced, and also check on memory and attention. We may also telephone call you over the course of the trial.

Step 4 Blood sample

You will be asked to provide three blood samples over the course of the trial. This part of the clinical trial is optional. However, should you consent to supplying blood samples, one sample will be taken at the start of the trial, one sample will be taken at the end of taking the experimental medicines (week 24) and one sample after completion of the main study (week 28). Each blood sample (taken in the standard fashion from a vein in your arm) will consist of 40 millilitres (4 tablespoons) of blood.

You may choose to take part in the clinical trial but not give blood samples. You may also choose to give blood samples for this clinical trial (provide specific consent), and also consent to have your blood stored for future ethically approved research (unspecified consent).

Will participating in the study cost me anything?

There are no additional costs associated with participating in this clinical trial. All medication, tests and medical care required as part of the study will be provided to you free of charge. To compensate you for your time and any inconvenience you will receive a $40 gift card at baseline, week 8, 16 and 24 (total of $160 worth of Coles/Myer gift vouchers).

What will happen to my samples?

The blood samples you donate will be sent to a dedicated research area for storage and later analysis. They will be used for this research study now (e.g. we will measure biochemical markers of oxidative stress in the blood that may be altered by mangosteen pericarp) and if you have consented, in the future. With your consent a 2 millilitre (< half a teaspoon) sample of blood

taken from you for future use will be shipped to the Stanley Medical Research Institute in the United States of America (USA) to be included in future world-wide studies of how new medications impact on various blood markers (e.g. markers of inflammation).

You will also have the option of providing consent to be part of other ethically approved studies conducted by The University of Queensland and or Queensland Health investigating mental illness. By consenting to participate in this clinical trial, you consent to the storage and later analysis and testing of your stored blood samples for the purposes noted above. With your consent, your biological material may be used in future years by scientists at The University of Queensland and or Queensland Health conducting ethically approved health related research.

Storage and disposal of your blood sample

All samples, (including the 2ml sample for the Stanley Medical Institute in the USA) we retain will be stored in a freezer in a dedicated research area and can only be accessed by authorised staff. They will be stored with your initials and participant number so that they are not identifiable while being stored. The master list of your name and participant number will be stored in a secure separate location. Any results of the analyses will be published as combined data, and will not be individually identifiable.

Future studies involving your stored blood samples will require approval from a Human Research Ethics Committee before they can commence to use your sample. If you consent to providing a blood sample for future research but decide at a later date you would like your sample destroyed, you may contact a member of the clinical trial team listed and this will be carried out. We plan to keep your blood sample along with your interview information for up to 15 years or the maximum time frame as determined by local regulations, whichever is the longest. After this time it will be destroyed.

What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this clinical trial; however you will be helping the research community test if mangosteen pericarp is be an effective 'add-on' treatment for schizophrenia. The benefit of mangosteen pericarp cannot be promised, nor can the

chance of benefit be accurately predicted. Participants usually find the tasks interesting, and enjoy being able to help advance our knowledge of better treatments for schizophrenia.

What are the possible risks and disadvantages of taking part?

There are some possible adverse effects or risks related to participation in this clinical trial which include:

(a) Very occasionally, talking about mental illness can be upsetting. If by chance the interview causes you discomfort, the interview will be stopped and support provided by a member of the clinical trial team to ensure your well-being. If you indicate a potential for self-harm or other serious risk, a member of the clinical trial team will report these responses immediately to the treating clinician.

(b) Clinical Assessments. The main inconvenience is the time spent completing these tasks. If you find the testing tiring, you can ask for a break, or complete this task over several sessions.

(c) Blood test. Complications associated with blood sampling are rare and minor, and may include local bruising and inflammation at the site of needle entry. Persons drawing blood have been trained in blood sampling techniques to minimize these complications.

(d) The effects of the dose of mangosteen pericarp used in this study on the unborn child and on the newborn baby are not known. Because of this, it is important that study participants are not pregnant or breast-feeding and do not become pregnant during the course of the study project. You must not participate in this clinical trial if you are pregnant, or trying to become pregnant, or breast-feeding. If you are female and becoming pregnant is a possibility, you will be required to undergo a pregnancy test prior to starting the clinical trial. Female participants are strongly advised to use effective birth control (chemical e.g. oral contraceptive pill or barrier e.g. condom) during the course of the clinical trial. If you do become pregnant whilst participating in the clinical trial you should advise a member of the clinical trial team immediately. Your trial clinician will withdraw you from the clinical trial.

(e) Mangosteen pericarp is generally recognised as safe.

What if new information becomes available?

Sometimes during the course of a clinical trial, new information becomes available about the treatment that is being studied. This new information may mean that you can no longer participate in this research. If this occurs, the person supervising the research will stop your participation. If new information does become available regarding mangosteen pericarp, you will be contacted to discuss whether you want to continue in the study. If you decide to continue in the study you will be asked to sign an updated consent form. Also, on receiving new information your trial clinician might consider it to be in your best interests to withdraw you from the trial. In all cases, you will be offered all available care to suit your needs and medical condition.

Can I have other treatments during this study?

You will be able to remain on all of your current treatments whilst participating in the trial. It is important to tell a member of the clinical trial team about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, or other alternative treatments. We ask you not to take non-study products that contain mangosteen extracts during the course of the study. You should also tell a member of the clinical trial team about any changes to these during your participation in the clinical trial to ensure your well-being and suitability to participate. It is essential that you are completely truthful regarding your health history and any symptoms or reactions you may experience during the trial. Your medical assessment and treatment will in no way be altered by your decision whether or not to take part, or by your answers to the questions. No additional tests, investigations or treatment will be involved other than those already described.

What type of questions will be asked?

The questions will be asked by a Registered nurse or psychologist and confidentiality will be maintained by the use of a number, allocated to you for all trial documentation. The questionnaires ask about your age, sex, marital, employment, housing status and, if any family members also have schizophrenia and to provide medical background of disease, length of time and nature of the illness. The questions are of a nature very similar to those you might routinely

be asked by your treating psychiatrist or nurses caring for you in hospital because of your schizophrenia or schizoaffective disorder. Additionally the nature of prescribed and complementary medication, exercise, dietary supplements that you are taking, any side effects will be asked.

What do I do if I wish to withdraw from the study?

Your participation in this clinical trial is voluntary. You may choose not to participate, or you may decide to withdraw your consent and discontinue your participation from this trial at any time without affecting current or future care. If you wish to withdraw from this study please advise the clinical trial team. You will be asked to complete and sign a "Revocation of Consent' form. This will be provided to you by the clinical trial team. If you wish to withdraw your consent, please notify a member of the clinical trial team immediately who will arrange a visit. As part of consenting to this clinical trial, you agree that the data you provide will be used for the clinical trial if you decide to withdraw. If you give blood samples and withdraw from the study, you may elect for your blood to be destroyed.

Could this study be stopped unexpectedly?

This clinical trial may be stopped unexpectedly for a variety of reasons. These may include reasons such as: unacceptable side effects, the drug being shown not to be effective for schizophrenia, and the drug being shown to work, and not needing further investigation. The trial clinician may end your participation in this clinical trial for any reason that they may feel is appropriate. These may include, but are not limited to, injury, a medical condition which may place you at risk of further complications if you continue to participate, failure to take the medication as instructed, or termination of the study by the investigators or for other administrative reasons.

What happens when the study ends?

Once the study is completed, the results will be grouped together, the code for who was receiving mangosteen or placebo is revealed, and then comparisons will be made between the two groups. These comparisons will be based on averages of each group and the results will not be able to identify any individual person. These results will be published in a scientific journal and presented at scientific and community forums. You will be provided a summary of these results including notification of which group of the study you took part in (mangosteen pericarp or placebo). It is

important to note that notification of which group you took part in cannot be made until all of the participants have completed the study.

What will happen to information about me?

Any information obtained in connection with this clinical trial that can identify you will remain confidential and will only be used for the purpose of this clinical trial and it will only be disclosed with your permission, except as required by law. The information collected is classified as re-identifiable. This means that details that identify you have been removed from the information (by replacing this information with a code), but that is possible to link the code back to you if necessary. The code will be stored separately from the data. The information collected from you in this clinical trial will be entered into a database, using the code rather than your personal identifiable details. However, the clinical trial team, regulatory authorities, and Metro South Human Research Ethics Committee (HREC) and site Governance, will be able to inspect and have access to confidential data that identifies you by name. As this is a multisite collaborative research clinical trial your de-identified data will be shared with researchers from other participating sites for purposes of analysis. Any analysis, interpretation and publication of the study results will not identify you.

Should you choose to consent for your blood to be stored for future research, the health information collected from you may be used in these studies. In this instance you are providing what is termed "unspecified consent" whereby you are consenting for your information to be used for any future research associated with your blood. The paper files from your interviews will be stored in locked filing cabinets in a dedicated research office. Computer files will be kept on a password-protected computer at each designated site (which has high level security). Only approved clinical trial staff, Metro South Research Ethics Committee, site Governance and the Therapeutic Goods Administration may access your data. Records relating to the results of the trial will be kept for 15 years. After the 15 year period your paper records will be shredded and destroyed and computer files deleted.

We may seek to review your health outcomes in future years via your medical records and Health Research Databases (e.g. Australian Institute of Health and Welfare). Should this occur, this will require approval from a Human Research Ethics Committee, and will not involve recontacting you personally. It will only involve your medical records or electronic health files.

How can I access my information?

In accordance with relevant Australian and/or State privacy and other relevant laws, you have the right to request access to the information collected and stored by the research team about you. You also have the right to request that any information with which you disagree be corrected. Please contact the research team member named in the question section of this document if you would like access to your information.

What if something goes wrong?

In the event that you suffer an injury as a result of participating in this trial, hospital care and treatment will be provided at no extra cost if you elect to be treated as a public patient at a public health service.

Who is organising and funding the study?

This clinical trial is being sponsored by The University of Queensland and the conduct of the clinical trial is overseen by the Coordinating Principal Investigator Professor John McGrath. The study has been funded by the Stanley Medical Research Institute in the USA.

Deakin University holds a patent for the use of mangosteen pericarp as a treatment for schizophrenia and Prof Michael Berk is listed as a co-inventor. This type of patent is called a method patent and it is not expected that there will be any monetary benefit from this patent

Who has reviewed the study?

All research in Australia involving humans is reviewed by an independent group of people, called a Human Research Ethics Committee (HREC). This clinical trial has been reviewed and given approval by Metro South Human Research Ethics Committee and site Governance.

How do I get more information?

You should ask for any information you want. If you would like more information about the study or if there is any matter about it that concerns you, either now or in the future, do not hesitate to ask one of the members of the clinical trial team or your doctor. Before deciding whether or not to

take part you may wish to discuss the matter with a relative or friend or with your doctor. You should feel free to do this.

If you have any questions about the study at any time, feel free to contact the researchers

Prof John McGrath	3271 8694
Andrea Baker	3271 8662
Toll free	1800 682 699
Fax	3271 8682
Email:	andrea_baker@qcmhr.uq.edu.au
	j.mcgrath@uq.edu.au

Postal Address QCMHR, The Park - Centre for Mental Health
Locked Bag 500 ARCHERFIELD BC QLD 4074

Ethical Guidelines and Independent Contact

This study has been approved by Metro South Human Research Ethics Committee and local site Governance, which is an appropriately constituted HREC under the National Health and Medical Research Council of Australia.

If you have any complaints about any aspect of the clinical trial, the way it is being conducted or any questions you can contact the Ethics Officer, Metro South Human Research Ethics Committee on 3443 8047 (phone); or EthicsResearch.PAH@health.qld.gov.au (email). All complaints will be treated in confidence, investigated fully and you will be informed of the outcome.

Participant Consent Form

Study Title The efficacy of adjunctive *Garcinia mangostana* Linn. (mangosteen) pericarp for the treatment of Schizophrenia (MANGO SZ)

- I have read , the Information Sheet and I understand the purpose of the clinical trial, what is involved, what data is being collected, any possible risks, inconveniences or discomforts involved, and what will be done with the data upon completion of the clinical trial.
- I have been given the time and opportunity to ask questions about the clinical trial and any questions I have asked have been answered clearly and to my satisfaction. I have also been given the opportunity to discuss this clinical trial with a person not connected to the clinical trial.
- I understand that all information provided by me is treated as strictly confidential and will only be shared with the clinical trial team and not be released by the clinical trial team unless required to do so by law.
- I know that I may withdraw from the trial at any time without having to give any reason or affecting my current or future medical treatment.
- I understand I will receive a copy of the participant information and signed consent form to keep.
- I understand and consent to those regulatory authorities and other organisations referred to in the participant information having access to my confidential information.
- I agree to participate in this research and give my consent voluntarily.

In addition: (optional initial next to your response)

- I give permission for a member of the clinical trial team to recontact me within the next 5 years regarding possible participation in further mental health research. Yes No
- I give permission for a member of the clinical trial team to notify my primary care physician and treating Psychiatrist of my participation in the study. Yes No
- I give consent for my blood to be taken at the time points specified for the purpose of this clinical trial. Yes No

- I give consent for 2ml's of my blood sample (at baseline and endpoint) to be shipped to Stanley Medical Institute in the United States of America (USA) to be included in future world-wide studies. Yes No
- I give consent for my blood samples to be stored and used for unspecified future testing, upon clearance by the relevant Human Research and Ethics Committee. Yes No
- I give consent for the research team to review my health outcomes via my medical records (paper and electronic) and Health Research Databases during the course of the current study. Yes No

_____	_____
Printed Name of Participant	Initial
_____	_____
Signature of Participant	Date (participant to date)
_____	_____
Signature of Witness	Date (witness to date)

REVOCATION OF CONSENT FORM

Full Project Title: The efficacy of adjunctive *Garcinia mangostana* Linn. (mangosteen) pericarp for the treatment of Schizophrenia (CADENCE-M)

I hereby wish to WITHDRAW my consent to participate in the clinical trial described above and understand that such withdrawal WILL NOT affect my current or future treatment.

As part of my original consent I agreed that my data would be used as part of the study, regardless of my decision to withdraw. However I have provided a blood sample and request that my sample be (initial all that apply):

- used for the purposes of this research project and/or;
- stored for future use as outlined in the participant information sheet
- destroyed after use for this research project
- destroyed immediately and not used for this research project or for future research projects

Participant's Name (printed) ……. Initial ……..

Signature…… Date……

Researcher's Name (printed)…….

Signature…… Date……