UNIVERSITY of MARYLAND
THE FOUNDING CAMPUS

RESEARCH CONSENT FORM

Protocol Title: Prebiotic Treatment in People with Schizophrenia

Study No.: HP-00081820

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- Before you agree to participate in this study, it is important that you read and understand the following explanation of the procedures.
- This statement describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study.
- Also described are the other procedures available to you, and your right to withdraw from the study at any time.
- It is important for you to understand that no guarantee or assurance can be made as to the outcome of your participation in this study.
- Please ask as many questions as you like before deciding to participate and during participation in this research study.
- Your participation in this study is voluntary.
- If you are court-ordered for treatment, or a prisoner, your participation in this study will have no effect on your release date, or parole.

PURPOSE OF STUDY

There will be about 30 people enrolled in this study at MPRC/Spring Grove Hospital Center. You are being asked to participate in this study because you have a diagnosis of schizophrenia or schizoaffective disorder.

The purpose this study is to examine if gut bacteria change levels of a fatty acid called butyrate after you receive 10 days of a prebiotic nutritional supplement in a drink or placebo (sugar like powder mixed in a drink); a prebiotic nutritional supplement is a natural plant fiber that beneficially nourishes the good bacteria already in the large bowel or colon.

Thirty patients at Spring Grove Hospital Center (SGHC) will be enrolled in this study; the study is being conducted by researchers from the Maryland Psychiatric Research Center (MPRC). You are being asked to participate in this study because you have a diagnosis of schizophrenia or schizoaffective disorder, and therefore, may have changes in the bacteria that normally live in

your intestine. These changes might worsen, or even cause the symptoms of schizophrenia or schizoaffective disorder. The bacteria in your intestines normally produce a small compound called butyrate, which is important for maintaining the healthy functioning of our intestines, and which seems to positively regulate our immune system, which fights infections and keeps us healthy. People with schizophrenia and schizoaffective disorder have been found to have reduced levels of butyrate, possibly leading to unhealthy intestines, an over-active immune system, and impaired brain functioning. Prebiotin is a natural plant fiber and nutritional supplement that is known to feed the healthy bacteria in our intestines that produce butyrate. By taking prebiotin, we might increase the production of butyrate in our intestines, and thereby improve the health of our intestines, our immune system, and our brain. The purpose of this study is to see if taking prebiotin for 10 days leads to an increase in butyrate in your blood.

PROCEDURES

Overview:

- If you agree to participate you will be enrolled in the study for about 3 and one-half weeks. This will include up to 2 weeks of an evaluation phase, when information is collected to make sure you are eligible to proceed in the study. IF you meet the study requirements, then you will proceed to a 10-day treatment phase.
- You will have your blood work drawn at the beginning and the end of the study. The total amount of blood drawn over the course of the study is approximately 10 tablespoons.
- You will collect stool samples at the beginning and the end of the study
- During the treatment phase, you will take either prebiotin or matching placebo 3 times a day for 10 days AND all participants will receive a prebiotin dose at the beginning and the end of the study.
- Neither you nor your doctor will know whether you are taking prebiotin or placebo for the 10 days in between the two doses.

Description of Evaluation Phase Visit(s): At the first evaluation phase visit, we will perform a standard medical workup including a physical exam, and EKG. We will collect blood for the following laboratory measures: CBC, Chemistry Panel, liver enzymes, and lipid panel.. The total blood drawn is about three tablespoons (about 45 ml). A urine sample will be collected for urinalysis and urine pregnancy test (if female). We will ask you questions about your medical, psychiatric, and smoking history. In addition, you will be shown how to collect stool samples. This visit will take about 3 to 4 hours and may be done over two or more days.

Description of the Treatment Phase Visits: If you meet inclusion criteria, you will be randomized to receive either the prebiotic nutritional supplement or placebo. Randomization is like the flip of a coin (a "50-50 chance") to determine whether you will be given the prebiotic or placebo. You will be given the prebiotic nutritional supplement, 3 times a day, with each of your meals, for 10 days. Your weight, height and vital signs (i.e., heart rate, pulse, and blood pressure) will

be assessed at the beginning and end of the 10 days. You will also have approximately 2 stool samples collected at the beginning and end of the 10 days.

In order to evaluate the impact of the prebiotic treatment on butyrate levels, we will test the ability of your gut bacteria to produce butyrate before and after treatment. There will be two test days: a) prior to treatment with prebiotic or placebo; and b) following the 10-day course of prebiotic or placebo treatment. On the night prior to the test day, you will receive a completely digestible and low fiber, e.g. lasagna. You will then fast from midnight until the morning, when you will receive your standard breakfast and a 12 gram dose of the prebiotic. Prior to your meal, we will collect blood for the following laboratory assessments: blood markers of inflammation, intestinal lining leakiness, and butyrate. Two and 6 hours after your meal, we will collect blood samples for butyrate. You will receive a light, low fiber meal 4 hours after you receive the prebiotin. ALL participants will receive the prebiotin dosing at baseline and endpoint.

We will repeat the same procedures after you complete the 10 day course of either the prebiotic or placebo. If any of these measures come back positive, then we will refer you for medical follow-up with the appropriate specialist, even if your participation in the study has ended. Any follow-up treatment with a specialist will not be part of the research study and you or your insurer will be responsible for any costs related to treatment. Please initial yes or no if you agree or do not agree to be contacted about follow-up treatment after your study participation has ended.
Yes_____ No_____

At the beginning of each test day, we will ask you questions about your symptoms. The total blood drawn for each test day is about five tablespoons (about or 75 ml.). At day 11, you will have a urine sample collected for analysis and if you are female, you will also have a urine pregnancy test completed. The total time for each test day visit will be about 7 hours.

WHAT ARE MY RESPONSIBILITIES IF I TAKE PART IN THIS RESEARCH?

If you take part in this research, you will be expected to: attend study visits as scheduled, consume the prebiotic or placebo as scheduled, follow protocol diet, allow for the drawing of blood samples, cooperate with obtaining stool samples, and take part in the study assessments.

POTENTIAL RISKS/DISCOMFORTS:

The major risks of this study are the risk for embarrassment from the collection of stool samples. You may have discomfort and bruising from the blood draw. You may find the symptom ratings and tests stressful, and possibly frustrating, boring, or upsetting. You may experience some embarrassment discussing personal information during interviews. You may ask to take a break at any time.

We are protecting your personal information but there is still a small risk that your research records would be viewed by someone not authorized to see it. To minimize this risk of someone being able to access your personal information, your research records will be kept in a secure location.
The prebiotic supplement is not absorbed into the body, but may cause gas or stomach discomfort in some people.

POTENTIAL BENEFITS

By providing blood and stool samples as part of the study, you may learn of abnormal results and be referred for treatment for conditions which would have otherwise gone undetected or evaluated. There is also the possibility that there will be no direct benefit from participating in the study, however the following clinical and research-related benefits may occur:

1) Potential clinical benefits for participation in the trial that are not present independent of study participation:
    a) You will have additional meetings with clinical and research staff for psychiatric symptoms and information and evaluation of study participation
    b) You will have access to life skills, illness education group, cognitive behavioral therapy and if a woman, women's trauma group during your stay
    c) You have the opportunity to spend Day 0 and Day 11 in the research suite. This provides access to private lounge, videogaming, quiet space and private time
    d) You will receive counseling on diet and can participate in healthy cooking groups

2) Potential research-related benefits for participation in the trial that are not present independent of study participation
    a) You will have extra visits for clinical symptom ratings. These include assessment of positive and negative psychiatric symptoms and assessments for anxiety symptoms. These are not routinely completed. The doctors will receive your full results of the symptom ratings and may help your doctor plan better treatment
    b) You will receive standard study assessments that are above and beyond routine care. These include EKG, additional vital signs and bloodwork
    c) You will be monitored daily for diet and food intake and the clinical staff will have access to full accountability of food intake for better and more personalized treatment planning
    d) You will have blood drawn for inflammatory markers (cytokines) and markers for the gut permeability. These are not routine laboratory measures. These results will help clinicians know if inflammation may play a role in your illness and if additional treatment strategies could potentially help their psychiatric symptoms.
    e) You will have a detailed medical history completed and have daily observation. You will receive referrals for advanced care if needed from any clinical or research findings.
    f) You will learn about prebiotin and will receive information about how to get this treatment if they wish to continue outside of the study.
    g) You will have assessments for adverse effects. This will include a private interview and asking of 25 adverse effects. These may or may not be study related but allows for you to discuss all issues you may be having and adverse effects that you are

dealing with. This information will help your doctor better address your problems which may not have been addressed previously. This may include constipation, indigestion, enuresis, etc.

Additionally, researchers may increase their understanding of whether, and how the activity of bacteria in the intestines affects the symptoms of schizophrenia. Your bowel movements may be more regular while taking the prebiotic nutritional supplement. This benefit could occur in either group as both will receive prebiotin at some point in the study.

ALTERNATIVES TO PARTICIPATION

You may choose not to participate in this study. If you choose not participate in this study, your treatment at any facility or clinic including MPRC and Spring Grove Hospital will not be affected.

You will be informed in a timely manner of any new findings which may affect your willingness to participate in this study.

COSTS TO PARTICIPANTS

It will not cost you anything to take part in this study.

PAYMENT TO PARTICIPANTS

You will receive $75 for completion of the evaluation phase visits and $50 for completion of the double-blind study visits. The total payment for study completion is $125.

You will be paid by cash or check. If paid by cash, then you will be paid at the end of each visit. If paid by check, then it may take up to 4-6 weeks to receive payment.

CONFIDENTIALITY AND ACCESS TO RECORDS

All forms with information about you will have only a code number and your initials, not your full name. With some exceptions, information that identifies you will not be given to people who are not working on this study, unless you give permission.

When you sign this consent form, you are letting us use your screening data (the information you provided when being screened for this study). Your signature also allows us to use the data that we collect during the study itself. We also ask for approval to contact you again in the future about this study, or other studies you may qualify for. Please initial yes or no if you agree or do not agree to be contacted.
Yes_____ No_____

The data from the study may be published. However, you will not be identified by name. People designated from the institutions where the study is being conducted auditors may be allowed to inspect sections of your medical and research records related to the study. Everyone using study information will work to keep your personal information confidential.

Efforts will be made to reveal your personal information, including research and medical records, only to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization. The monitors, auditors, and the IRB will be granted direct access to your medical records for verification of the research procedures and date. By signing this document, you are authorizing this access.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

RIGHT TO WITHDRAW

Your participation in this study is voluntary. You do not have to take part in this research. You are free to withdraw your consent at anytime. Refusal to take part or to stop taking part in the study will involve no penalty or loss of benefits to which you are otherwise entitled and will not adversely affect your treatment at MPRC, University of Maryland or Spring Grove Hospital. If you decide to stop taking part, if you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact the principal investigator, Robert W. Buchanan at 410-402-7876.

There are no adverse consequences (physical, social, economic, legal, or psychological) of your decision to withdraw from the research. If you wish to no longer participate in the study, please notify a member of the research team. The results from the research will not provide information on your health. You will not receive any individual results.

If you withdraw from this study, already collected data may not be removed from the study database.

CAN I BE REMOVED FROM THE RESEARCH?

The person in charge of the research study, the medically responsible physicians or the agencies that monitor the study can remove you from the research study without your approval. Possible reasons for removal include failure to follow instructions of the research staff, if the person in charge decides that the research study is no longer in your best interest, or you are unwilling or unable to comply with the research schedule. The study doctor will tell you about this and you will have the chance to ask questions if this were to happen.

UNIVERSITY STATEMENT CONCERNING RESEARCH RISKS

The University of Maryland, Baltimore (UMB) is committed to providing participants in its research the rights due them under State and federal law. You give up none of your legal rights by signing this consent form or by participating in the research project. This research has been reviewed and approved by the Institutional Review Board (IRB). Please call the Institutional Review Board (IRB) if you have questions about your rights as a research subject.

Participating in research may result in an injury, as explained above. If you suffer an injury directly related to your participation in this project, UMB and/or one of its affiliated institutions or health care groups will help you obtain medical treatment for the specific injury and provide referrals to other health care facilities, as appropriate. UMB and/or its affiliated institutions or health care groups will not provide you with financial compensation or reimbursement for the cost of care provided to treat a research-related injury or for other expenses arising from a research-related injury. The institution or group providing medical treatment will charge your insurance carrier, you, or any other party responsible for your treatment costs. If you incur uninsured medical costs, they are your responsibility. The study staff can give you more information about this if you have a study injury.

By signing this Consent Form, you are not giving up any legal rights. If this research project is conducted in a negligent manner and you are injured as a direct result, you may be able to recover the costs of care and other damages from the individuals or organizations responsible for your injury.

If you have questions, concerns, complaints, or believe you have been harmed through participation in this research study as a result of researcher negligence, you can contact members of the IRB or the Human Research Protections Office (HRPO) to ask questions, discuss problems or concerns, obtain information, or offer input about your rights as a research participant. The contact information for the IRB and the HRPO is:

University of Maryland Baltimore
Human Research Protections Office
620 W. Lexington Street, Second Floor
Baltimore, MD 21201
410-706-5037

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

If you agree to participate in this study, please sign your name below.

_____	_____
Participant's Signature	Designee Obtaining Consent Signature
Date:_____	Date:_____
_____	_____
Investigator	Witness
Date:_____	Date:_____