UNIVERSITY OF CALGARY

RESEARCH INFORMATION SHEET

Name of Study: **Effect of Prebiotic Fibre on Glycemic Control, Gut Microbiota, and Intestinal Permeability in Newly Diagnosed (<12 months) Type 1 Diabetes**

Who is Eligible: Children that have been newly diagnosed with Type 1 Diabetes within the previous 12 months

Brief Description:

Can taking a prebiotic fiber supplement improve diabetes control and prolong honeymoon?

If you are interested in joining this study or would like more information please contact Tetsuro Okada at:
403-955-7758 or **tetsuro.okada@albertahealthservices.ca**

Can taking a prebiotic fiber supplement improve diabetes control and prolong honeymoon?

Your child could be part of this study if:

- Diagnosed with type 1 diabetes in the past 12 months
- Between the ages of 7 years - 17 years old

This study involves:

- Taking a fiber supplement for 6 months
- Completing questionnaires
- Blood, urine and stool samples at baseline, 3 months and 6 months to coordinate with usual blood tests for diabetes

If you are interested in joining this study or would like more information please contact Tetsuro Okada at: 403-955-7758 or tetsuro.okada@albertahealthservices.ca

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Poster Version Date: Version 4.0, May 4, 2022
This study has been approved by the University of Calgary Conjoint Health Research Ethics Board (Ethics ID # REB21-0852*)*

Type 1 Diabetes and Fiber Study
Research Coordinator
403-955-7758
tetsurookada@albertahealthservices.ca

UNIVERSITY OF CALGARY
PARENT CONSENT FOR CHILD TO PARTICIPATE IN RESEARCH

TITLE: Effect of Prebiotic Fibre on Glycemic Control, Gut Microbiota, and Intestinal Permeability in Newly Diagnosed (<12 months) Type 1 Diabetes

SPONSOR: University of Calgary

FUNDER: Canadian Institutes of Health Research

INVESTIGATORS: Dr. Raylene Reimer, Dr. Carol Huang, Dr. Josephine Ho, Dr. Sonia Butalia. Phone number: 403-220-8218.

INTRODUCTION

Dr. Raylene Reimer, and associates from the Alberta Children's Hospital and the Department of Pediatrics at the University of Calgary are conducting a research study.

This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your child's participation will involve. If you would like more detail about something described here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information.

Your child was identified as a possible participant in this study because they have been diagnosed with type 1 diabetes in the last 12 months. Your child's participation in this research study is voluntary.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to determine whether a dietary fibre supplement can improve glucose control (highs and lows in blood glucose) in persons who have been diagnosed with type 1 diabetes within the past 12 months. Prebiotic fibre is a unique type of dietary fibre with the potential to be an inexpensive, low-risk treatment addition for type 1 diabetes. The fibre may improve blood glucose control through changes in gut microbiota (bacteria), gut permeability (leaky gut), and inflammation. The gut microbiota is increasingly recognized as a contributor to various diseases in

people. Both animal and human studies found a difference in gut bacteria profiles between those that develop diabetes from those that did not develop diabetes. Prebiotic fibre may help correct defects in the gut microbiota associated with type 1 diabetes. Prebiotic fibre has also been shown to improve blood glucose levels and reduce inflammation markers in the body. A small initial study in children with type 1 diabetes showed that prebiotic fibre could increase C-peptide levels in the blood, which is a marker that reflects the ability of the pancreas to still produce some insulin. The study also showed that prebiotic fibre might be able to reduce episodes of hypoglycemia (low blood sugar).

The current study is a larger scale version of the small initial study. In this study we will recruit patients from the Alberta Children's Hospital and randomize (like a flip of a coin) participants with type 1 diabetes to receive either the prebiotic fibre powder or a non-active ingredient (placebo). This study is double-blinded (researchers and participants don't know who is receiving the fibre or placebo). This blinding can be broken should an emergency arise and you or your child's treating physician requires the information.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 144 people will take part in this study in Alberta and Saskatchewan. About 100 people will take part in this study through the University of Calgary.

WHAT WILL HAPPEN IF MY CHILD TAKES PART IN THIS RESEARCH STUDY?

If you agree to allow your child to participate in this study, we would ask them to:

At Baseline Visit:

1. **Questionnaire** (age, gender, diagnosis details including date of type 1 diabetes diagnosis, current medications, other medical conditions, number of episodes of severe hypoglycemia and diabetic ketoacidosis since diagnosis of type 1 diabetes). Some of this information will be collected from your child's medical chart since it may be a lot of details to remember.
2. **Measurements** (height, weight)
3. **Surveys** that include a Fear of Hypoglycemia survey, Quality of Life survey, and a 24-Hour Diet Record
4. **Continuous blood glucose monitoring** will be done for a minimum of 3 weeks prior to your child's baseline visit. A Dexcom G6 will be provided to you if you do not have one. The data from your child's continuous glucose monitor and their self-monitored blood glucose logs will be collected at the clinic visit.
5. **Blood sample** coordinated with usual diabetes clinic bloodwork (HbA1c, inflammatory markers). Results from the HbA1c test will be collected from your child's medical chart.
6. **Gut leakiness test.** Your child will consume a regular evening meal and then 3 hours prior to bedtime drink a solution containing lactulose (5g), mannitol (2g)

and 3-O-methylglucose (5g) in 200 mL of water. All urine for the following 12h will be collected in a storage container and you will bring the container to the clinic within 24 hours.

7. **Meal tolerance test.** Your child will arrive to clinic fasted. You will get special instructions about diet and changes to insulin dosing to ensure consistency before the test. To make the blood sampling easier for the test, an intravenous needle and plastic tube (IV) will be placed in your child's vein. The IV will be kept in place during the test so your child only gets poked once. One blood sample (one teaspoon of blood) will be taken through the IV. You will then drink a meal replacement beverage (like "Boost"). Additional blood samples will be drawn through the IV at regular intervals for 2 hours to measure glucose and hormones that tell us how well your child's body is making insulin (C-peptide, glucose, insulin, proinsulin).
8. **Stool sample** will be collected at home. Two tablespoons of stool will be placed in a pre-labelled sterile conical tube, placed in a plastic bag and stored in your home freezer (-20°C). Stool samples will be brought to the laboratory on ice within 1 week from collection and stored at -80°C until analysis.

At Randomization:

1. Your child will be randomized to receive either placebo (maltodextrin) or prebiotic fibre (oligofructose-enriched inulin) for 6 months.
2. Both prebiotic fibre and placebo come in a powder form.
3. You will be instructed to mix the powder with 250 mL water until dissolved. We suggest taking it with the evening meal.
    i. For the first 3 weeks, your child will be asked to only take half of the dose in order to minimize potential intestinal side effects (e.g. increased gas) and then you will take the full dose for the remainder of the 6 month study.
    ii. You will be asked to record any diabetes related adverse reactions (i.e. severe hypoglycemia and diabetic ketoacidosis).
    iii. At the end of the 6 months, you will be asked to return any remaining placebo or prebiotic in order to assess for compliance.

After 3 months (half-way through the study):

- Your child will be asked to repeat all the tests and surveys that were done at baseline.

After 6 months (end of study):

- Your child will be asked to repeat all the tests and surveys that were done at baseline.

Telephone contact from a member of the research team will occur twice a month to encourage your child to take the study product every day and for recording of any reactions, especially hypoglycemia and intestinal symptoms (i.e. gas, bloating, change in stool frequency or quality).

WHAT WILL HAPPEN WHEN MY CHILD FINISHES THE STUDY?

When your child completes the study, they will continue to see their usual diabetes doctor for their regular care. If the fibre proves to be beneficial and your child was randomly assigned to the placebo, you will be offered a supply of the fibre for your child to try on their own. There are no tests associated with your child using the fibre after the study.

HOW LONG WILL MY CHILD BE IN THE RESEARCH STUDY?

The study will include a minimum of four visits over the course of 6 months. Taking into account the screening visit, baseline visit and visits at 3 and 6 months as well as filling out the questionnaires and tests at home, it is estimated that you and your child will spend at least 15 hours over the next 6 months on this study.

ARE THERE ANY POTENTIAL RISKS OR DISCOMFORTS THAT MY CHILD CAN EXPECT FROM THIS STUDY?

The fibre can sometimes cause intestinal side effects (e.g. gas, bloating, change in stool, mild abdominal pain). For the first three weeks, your child will be asked to only take half of the dose in order to minimize potential side effects and then take the full dose for the remainder of the 6 month study. Your child could have discomfort and/or a bruise when they get their blood drawn but these would be brief and transient. There is a minimal chance of infection. The Meal Tolerance Test requires drinking a product which contains milk and soy ingredients. If your child has a known allergy to either of these ingredients, please let us know.

ARE THERE ANY POTENTIAL BENEFITS TO MY CHILD IF THEY PARTICIPATE?

If you decide to have your child participate in this study, there may or may not be a direct medical benefit. Your child's type 1 diabetes may be improved during the study but there is no guarantee that this research will help. The information we get from this study may help us to provide better treatments in the future for patients with type 1 diabetes.

WHAT OTHER CHOICES DOES MY CHILD HAVE IF THEY DO NOT PARTICIPATE?

If you decide against your child taking part in this study, your child will receive the usual standard of care from their medical team. Your child will continue to have regular treatments through the diabetes clinic and their usual diabetes team. Participation in this study is voluntary and you/your child may withdraw from it at any time without jeopardizing your child's health care.

CAN MY CHILD STOP BEING IN THE STUDY?

Yes. You can decide to stop your child's participation at any time. Tell the study investigator if you are thinking about stopping or decide to stop your child's participation. If you stop, your child will continue their regular diabetes care with their diabetes doctor.

CAN THE RESEARCHERS REMOVE MY CHILD FROM THIS STUDY?

The researchers may end your child's participation in this study for a number of reasons, such as if your child's safety and welfare are at risk, if your child does not follow instructions or if your child misses scheduled visits. The researchers or the study sponsor might also decide to stop the study at any time.

If you decide to stop your child's participation in the study, or your child is removed from the study, or the study is stopped, the researcher will ask your child to have a brief telephone conversation with the research coordinator.

WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT MY CHILD?

During the study, the researchers could learn something about your child that they didn't expect. For example, the researchers may find out that your child has another medical condition. The researchers will consult with medical experts as needed to evaluate the findings and will then share these results with you. You will be helped with arranging appropriate follow up and care for your child.

I consent for the researchers to share findings about my child with me:

- ❑ YES
- ❑ NO

WITHDRAWAL OF STUDY DATA

If you decide to stop being in the study, or are removed from the study, or the study is stopped, the data collected about your child up to that point will remain part of the study because withdrawal of data in clinical trials could bias results.

WILL MY CHILD BE PAID FOR PARTICIPATING, OR DO I HAVE TO PAY FOR ANYTHING?

You will be reimbursed for the cost of parking at each study visit. A $25 Chapters or Amazon gift card will be given to your child when they complete the study to thank them for their participation.

WILL INFORMATION ABOUT MY CHILD'S PARTICIPATION BE KEPT CONFIDENTIAL?

The researchers will do their best to make sure that your child's private information is kept confidential, unless required by law. Information about your child will be handled as confidentially as possible, but there is always the potential for an unintended breach of privacy. The research team will handle data according to the Data Management Plan as outlined below:

Only the researchers and designated research assistants will have access to the information collected. All identifiable information about your child will be replaced with a study code. A master list linking the study code and your child's identifiable information will be kept separate from the research data. All paper files will be kept in locked offices at the Alberta Children's Hospital and/or University of Calgary. All data will be password protected and stored on a University of Calgary server.

Authorized representatives from the University of Calgary and the Conjoint Health Research Ethics Board may look at your child's research records held at the University of Calgary for quality assurance purposes. By signing this form you are authorizing such access.

HOW LONG WILL INFORMATION FROM THE STUDY BE KEPT?

The researchers intend to keep the research data and records for a minimum of five years. Data collected for this study may be shared with other researchers for future studies that are unknown at this time. Any data shared with other researchers, will not include your child's name or other personal identifying information. Any future use of this research data is required to undergo review by a Research Ethics Board.

WHAT OTHER THINGS SHOULD I CONSIDER BEFORE MY CHILD PARTICIPATION?

Use of My Child's Specimens:

Any specimens (e.g., blood, urine, stool) obtained for the purposes of this study will become the property of the University of Calgary. Once your child provides the specimens you and your child will not have access to them. The University may share your child's specimens in the future with other researchers or outside institutions. Information that identifies your child will not be shared with anyone outside of the University of Calgary. The specimens will be used for research and such use may result

in inventions or discoveries that could become the basis for new products or diagnostic or therapeutic agents. In some instances, these inventions and discoveries may be of potential commercial value and may be patented and licensed by the University. You and your child will not receive any money or other benefits derived from any commercial or other products that may be developed from use of the specimens.

RESEARCHER CONFLICTS OF INTERESTS

The study is funded by the Canadian Institutes of Health Research which has no financial interest in its outcome. Payments are made to the University of Calgary and are used to cover the expenses of the study. The investigators do not have a financial interest in the outcomes of the study. The principal investigator, Dr. Raylene Reimer, has received a speakers honorarium in the past for a conference presentation about prebiotic fibre.

USE OF DATA AND SPECIMENS FOR FUTURE RESEARCH

My child's research data and/or specimens may be kept for use in future research to learn about, prevent or treat other health-related problems.

- ❑ YES
- ❑ NO

CONTACT FOR FUTURE RESEARCH

University of Calgary researchers may contact me in the future to ask my child to take part in other research studies.

- ❑ YES
- ❑ NO

IF MY CHILD SUFFERS A RESEARCH-RELATED INJURY, WILL WE BE COMPENSATED?

It is important that you tell the researchers if you believe that your child has been injured because of taking part in this study. In the event that your child suffers injury as a result of participating in this research, no compensation will be provided to you by the Canadian Institutes of Health Research, the University of Calgary, Alberta Health Services or the Researchers. However, you still have all your legal rights. Nothing said in this consent form alters your right to seek damages.

WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

The Research Team:
You may contact Dr. Raylene Reimer at 403-220-8218 with any questions or concerns about the research or your child's participation in this study.

Conjoint Health Research Ethics Board (CHREB):
If you have any questions concerning your child's rights as a possible participant in this research, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

Public Information about this Study:
ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify your child. At most, the website will include a summary of the results. You can search this website at any time.

HOW CAN I FIND OUT ABOUT THE STUDY RESULTS?

Once the study data is analyzed and published, the study investigators can provide you with a link to the publication.

WHAT ARE MY CHILD'S RIGHTS IF THEY TAKE PART IN THIS STUDY?

Your child's participation in this study is a choice. You can choose whether or not you want your child to participate. Whatever decision you make, there will be no penalty to you or your child.

- You have a right to have all of your questions answered before deciding whether your child will take part.
- Your decision will not affect the standard medical care your child receives.
- If you decide for your child to take part, they can leave the study at any time.
- Your child may refuse to answer any questions that they do not want to answer and still remain in the study.

HOW DO I INDICATE MY AGREEMENT FOR MY CHILD TO PARTICIPATE?

Your signature on this form indicates that you have understood to your satisfaction the information regarding your child's participation in the research project and agree for them to participate as a participant. In no way does this waive your or your child's legal rights nor release the investigators or involved institutions from their legal and professional responsibilities.

Name of Child

SIGNATURE OF PARENT OR LEGAL GUARDIAN

Name of Parent or Legal Guardian

Signature of Parent or Legal Guardian | Date

SIGNATURE OF PERSON OBTAINING CONSENT

Name of Person Obtaining Consent | Contact Number

Signature of Person Obtaining Consent | Date

SIGNATURE OF THE WITNESS

Name of Witness

Signature of Witness | Date

A signed copy of this consent form has been given to you to keep for your records and reference.

UNIVERSITY OF CALGARY
GENERAL ASSENT TO PARTICIPATE IN RESEARCH

TITLE: Effect of Prebiotic Fibre on Glycemic Control, Gut Microbiota, and Intestinal Permeability in Newly Diagnosed (<12 months) Type 1 Diabetes

SPONSOR: University of Calgary

FUNDER: Canadian Institutes of Health Research

INVESTIGATORS: Dr. Raylene Reimer, Dr. Carol Huang, Dr. Josephine Ho, Dr. Sonia Butalia. Phone number: 403-220-8218.

INTRODUCTION

A research study is a way to find out new information about something. People don't need to participate in a research study if they don't want to participate.

You can talk this over with your parents before you decide whether or not to participate. We will also ask your parents to give their permission for you to take part in this study. But even if your parents say "yes" you can still decide not to do this.

WHY IS THIS STUDY BEING DONE?

You are being asked to take part in this research study because we are trying to learn more about type 1 diabetes and if eating more fibre helps with blood sugars. We are asking you to be in the study because you have type 1 diabetes. About 144 people will be in this study.

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

If you decide to take part in this study, here are some things that will happen:
You will be asked to drink a glass of water with fibre in it every evening for 6 months. To see if the fibre did its job, we need to do some tests on your urine (pee), stool (poop) and blood. There are 3 study visits when we will do these tests. Just before each visit, we want you to take a special drink. Then we want you or your parents to keep some of your urine (pee) and your stool (poop) and bring it with you to the visit. We would also

take extra blood from your regular blood test for diabetes. There should not be any extra needle for this little extra blood but there is one more blood test where we will get you to drink something called Boost that tastes like flavored milk. We will take a little blood at 6 times after you drink the Boost. We only need to poke you with a needle once though because we use a very small little tube that stays in your arm for the whole test. We will ask you some questions at each of your visits about how you feel about your diabetes.

The study is 6 months long and you will be asked to do the tests 3 times. That means testing at the beginning, the middle and the end of the 6-month study.

ARE THERE ANY POTENTIAL RISKS OR DISCOMFORTS THAT I CAN EXPECT FROM THIS STUDY?

The fibre you would be drinking every evening can sometimes make people have more gas, feel full, or a little bit of tummy pain which should go away once your body is used to the extra fibre. The special drink you will have before you collect your urine should not have any bad effect on your body, but if people drink a lot more of it, it can make their poop watery and their stomach feel full. We will take about 2 tablespoons of blood when you come in for your tests every 3 months. Sometimes you might get a little bruise in your arm where the blood was taken.

WILL THE STUDY HELP OTHERS?

This study might find out things that will help other people with diabetes some day.

WHO WILL SEE THE INFORMATION COLLECTED ABOUT ME?

The information collected about you during this study will be kept safely locked up. Nobody will read it except the people doing the research. The study information about you will be given to your parents. The researchers won't tell your friends or anyone else that you are in this study, or share any information about you.

DO I HAVE TO BE IN THE STUDY?

You don't have to be in the study. It is up to you. No one will be upset if you don't want to do this study. You can say yes, or you can say no. You can also take more time to think about being in the study.

If you want to stop, then all you have to do is tell us you want to stop. No one will be mad at you if you don't want to be in the study, or if you say yes now then want to stop later.

WHAT DO I GET FOR BEING IN THE STUDY?

You will get a $25 gift card to Chapters or Amazon for finishing the study.

WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

The Research Team:
You can ask any questions that you may have about the study. If you have a question later that you didn't think of now, either you can call or have your parents call Dr. Raylene Reimer at 403-220-8218. You can also take more time to think about being in the study and also talk some more with your parents about being in the study.

WOULD YOU LIKE TO BE IN THIS RESEARCH STUDY?

If you decide to be in the study, then please write your name below. You can change your mind and stop being part of the study at any time. All you have to do is tell us. It's okay. The researchers and your parents won't be upset with you

❑ Yes, I want to be in this study. ❑ No, I don't want to do this.

_____
Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF PERSON OBTAINING ASSENT

_____
Name of Person who received assent

_____ _____
Signature of Person who received assent Date

You will be given a copy of this paper to keep.

UNIVERSITY OF CALGARY
ASSENT FOR CHILD TO PARTICIPATE IN RESEARCH

TITLE: Effect of Prebiotic Fibre on Glycemic Control, Gut Microbiota, and Intestinal Permeability in Newly Diagnosed (<12 months) Type 1 Diabetes

SPONSOR: University of Calgary

FUNDER: Canadian Institutes of Health Research

INVESTIGATORS: Dr. Raylene Reimer, Dr. Carol Huang, Dr. Josephine Ho, Dr. Sonia Butalia. Phone number: 403-220-8218.

My name is Dr. Raylene Reimer.

We want to tell you about a research study we are doing. A research study is a way to learn more about something. We want to find out more about diabetes and if eating more fibre helps with blood sugars. We are asking you to be in the study because you have type 1 diabetes. About 144 children will be in this study.

We want to tell you about some things that will happen to you if you are in this study. You will be asked to drink a glass of water with fibre in it at supper everyday. To see if the fibre did its job, we need to do some tests on your urine (pee), stool (poop) and blood. We need to do these tests at 3 different visits. Just before each visit, we want you to take a special drink. Then we want your parents to keep some of your urine (pee) and your stool (poop) and bring it to us. We would also take extra blood from your regular blood test for diabetes. There should not be any extra needle for this little extra blood but there is one more blood test where we will get you to drink something called Boost that tastes like flavored milk. We will take a little blood at 6 times after you drink the Boost. We only need to poke you with a needle once though because we use a very small little tube that stays in your arm for the whole test. We will ask you some questions at each of your visits about how you feel about your diabetes. The study is 6 months long and you will be asked to do the tests 3 times.

The fibre you would be drinking every evening can sometimes make people have more gas, feel full, or a little bit of tummy pain which should go away once your body is used to the extra fibre. The special drink you will have before you collect your urine should

not have any bad effect on your body, but if people drink a lot more of it, it can make their poop watery and their stomach feel full. We will take about 2 tablespoons of blood when you come in for your tests at the 3 visits. Sometimes you might get a little bruise in your arm where the blood was taken.

We don't know if being in this study will help you but your blood sugars may get better. We might find out things that help other children with diabetes some day.

You don't have to join this study. It is up to you. You can say yes or you can say no. It's OK if you say yes and then you change your mind later. If you want to stop, then all you have to do is tell us or your parents you want to stop. No one will be mad at you if you don't want to be in the study or if you say yes now then want to stop later.

Before you say yes or no to being in this study, we will answer any questions you have. If you join the study, you can ask questions at any time. Just tell us or your parents that you have a question.

We will also talk to your parents about this study. You can talk this over with them before you decide.

If you have a question later that you didn't think of now, you can call or have your parents call Dr. Raylene Reimer at 403-220-8218.

WOULD YOU LIKE TO BE IN THIS RESEARCH STUDY?

❑ Yes, I want to be in this study. ❑ No, I don't want to do this.

_____ _____
Name of Child Date

_____
Name of Person who received assent

_____ _____
Signature of Person who received assent Date

You will be given a copy of this paper to keep.