

**A randomized controlled trial of the effect of replacing sugar-sweetened beverages with non-nutritive sweetened beverages or water on gut microbiome and metabolic outcomes: Strategies To OPpose SUGARS with Non-nutritive sweeteners Or Water trial
NCT03543644**

Genetic ICF version 2

2018 Dec 28

LETTER OF INFORMATION AND CONSENT TO PARTICIPATE IN A RESEARCH SUB-STUDY

You are being asked to consider taking part in a research sub-study. Before agreeing to take part in this research sub-study, it is important that you read the information in this research consent form. It includes details we think you need to know in order to decide if you wish to take part in the sub-study. If you have any questions, ask the study doctor or study staff. You should not sign this form until you are sure you understand the information. All research is voluntary. You may also wish to discuss the sub-study with your family doctor, a family member or close friend. If you decide to take part in the sub-study, it is important for your safety and for the conduct of the sub-study that you are as accurate as possible about your health history and any medications you are taking.

**Title of Research Study: Strategies To OPpose SUGARS with Non-nutritive Sweeteners Or Water (STOP SUGARS NOW) Trial (REB# 17-292)
-Long-Term Banking and Genetic Testing (optional)**

Consent for this section of the sub-study is optional but we hope it is of sufficient interest to allow all those who enroll in the main study to also be included in this “sub-study” for which no extra blood, fecal, urine samples or effort is required.

BACKGROUND AND PURPOSE

General:

To create a biobank (long-term storage of biological samples including urine, feces, and blood) to be able to explore risks and markers of diabetes and heart disease when new tests are discovered.

To also determine whether there are differences between individuals in their response to dietary change, e.g. do some people respond better to drinking diet pop instead of regular pop, and risks of diabetes and heart disease.

Specific: The long-term banking and genetic sub-study are **optional** components of the study in which you have enrolled as a participant.

Once we have funding approved, the purpose of the long-term banking is store biological samples from many of our studies to be able to test for risks and markers of diabetes and heart disease once new procedures are discovered or additional funding is given.

The genetic component's purpose is to see whether there are genetic differences between you and other people, which might determine how you respond to dietary changes in the context of risks of diabetes and heart disease. There is considerable interest in the scientific community to see if, for example, some people are more or less likely to have different food cravings (such as salt or sweet). Our eventual hope is that, on the basis of studies such as this, we will be able to direct people like you to the best diet for you based on an assessment of diet related genes. Obviously we are only at the beginning now and the knowledge we gain, though very valuable for the future, may have little immediate use. Our hope is that this will not be entirely the case but only the outcome of this research may allow us to tell.

DESCRIPTION OF THE RESEARCH

The aim of this sub-study is to collect biological samples for future analysis to including to see how genes may influence response to diet.

No additional blood, urine, or fecal samples are required as we will make use of the samples that you are already providing. The long-term storage will keep any remaining samples. The DNA (genetic

material) can be extracted from the blood samples (white cells – “buffy coat”) already collected from you.

The analysis done with your long-term storage biological samples will only explore risks and markers of diabetes and heart disease. The genetic analysis will only explore genetic variations that may affect risks and biomarkers of diabetes and heart disease. The intended analysis should not produce any incidental findings that would be clinically actionable. However, if we do find anything that is clinically relevant we will contact you based on what you consent to at the end of this form. We will be looking at specific genes that are known to be associated with dietary responsiveness or unresponsiveness. The genes of interest will be those that may relate to the effectiveness of dietary change on blood glucose and cholesterol. We will also look at genes that may be associated with other measurements including blood pressure, taste preference, compliance (this will include genes that are related to satisfaction, a sense of being rewarded and may relate to the need for increased food, especially carbohydrate food intake). Generally, the effect of genes on diet is very modest and usually requires significant numbers of people. It therefore has very limited clinical relevance. However, if we discover specific groups for which certain types of dietary advice may prove advantageous, this will be communicated to you at the end of the sub-study, with your consent.

The samples taken from your remaining blood, urine, or fecal samples from the main study will be stored at the University of Toronto for up to 30 years or until all the samples have been used for analyses and no further sample remains. Storing your samples will allow the study investigators to perform additional testing, including genetic analysis of your blood in the future. All additional testing which will be performed will be within the scope of this sub-study. Our research group does not know (at the time of your signing this form) which tests may be performed in the future. During the course (3+ years) of the main study we will seek your consent if we decide to do whole genome testing. If you are no longer in the study at this time we will contact you to obtain your consent. Apart from this we will not continue to contact you after the completion of the main study but you are welcome to contact the university or hospital study office to see if any new information has emerged from subsequent analyses.

All remaining samples will be destroyed by autoclaving (heating) at the end of 30 years. You have the option of consenting to this long term storage of your samples for use in future research for the assessment of genes of interest that may advance our knowledge in the relationship between diet and chronic disease.

The sub-study results will be submitted for publication in the medical/scientific literature. No information which could identify you will be included in any publication. The samples will be used only for the purposes stated in this consent form.

Any exploration of genetic variations or findings from long-term storage analysis will not impact your current or future treatment(s) at St Michael's Hospital, your relationship with the University of Toronto, or any future contact with the study physicians.

NEW INFORMATION ABOUT YOUR HEALTH (INCIDENTAL FINDINGS)

During research, medical information about you may be found. This type of medical information is called an incidental finding and is defined as any information concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims and objectives of the research. Medical information that is not helpful to your health care (like most genetic research information) will not be shared (except if

required by a government agency or other legal authority). At the end of this form you may choose to consent to having any medical findings released to you or your family doctor.

At any time, you may ask the study doctor to see your personal information and correct it, if necessary. In some circumstances, you may not be able to access your study information while the study is ongoing. The study doctor will share any important medical information, including any incidental findings, if it is relevant to your health during the course of the study.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS SUB-STUDY?

There are some risks associated with this sub-study. With any clinically relevant genetic findings related to diabetes and heart disease, you may experience some psychological distress, dependent on the results. While we do our best to minimize the release of data, there is always the risk that it does get released. This could potentially impact insurance policies. However, as described in the below confidentiality section, we work to keep your information confidential and safe. Since the aim of the sub-study is to see how specific genes may influence your response to diet. The limited diet-related findings will be preliminary and we can only share speculations on what might be a good dietary approach for that person's genes. We therefore do not believe genetic counseling is required. However, we hope to make any incidental findings known to participants at the end of the sub-study, especially if we discover specific groups of people for whom certain types of dietary advice may prove advantageous. The samples will be used only for the purposes stated in this consent form.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS SUB-STUDY?

You will not benefit directly by participating in this sub-study. In the long term, this sub-study may allow more individually tailored dietary and lifestyle advice to be given, so that diet may be more effective in preventing cardiovascular disease, diabetes and other chronic diseases.

HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL?

Your genetic information will be kept separate from your name. There is a possibility that the genetic tests may re-identify you but the risk of your other biological samples identifying you is very low; however, we are managing the samples in the following way to ensure that this risk is minimized:

The genetic data and biological samples will be linked by your study ID number to all the health information acquired in the study (e.g. age, sex, height, weight, blood pressure and glucose and cholesterol related measurements, plus all the dietary data). The genetic data and biological samples will therefore be linked to the diet and biochemical data with only your study ID as the identifier. Your genetic data are unlikely to have impact that would justify inclusion in your medical records and we have no plans to do so.

Blood samples will be stored and analyzed at the University of Toronto laboratories (Toronto, Ontario, Canada) or at other specialized academic centres: for example, the laboratories of collaborating investigators in universities in Ontario, Quebec, Manitoba and British Columbia. The genetic and biological samples will be in freezers in a locked room only accessible by trained study staff. The samples will only have your study ID on them. Once we have secured funding to set up our biobank, our freezers will have a locking system as well as another measure of security. It is possible that samples may be sent outside Canada if a centre has the relevant expertise, but we have no plans to do so at present. Your samples will be de-identified, meaning that these will not have any personal information that could identify you in any way (such as your name or date of birth).

Our research group does not know (at the time of your signing this form) which exact tests and genetic tests may be performed in the future. During the course (3+ years) of the main study we will seek your consent if we decide to do whole genome testing. If you are no longer in the study at this time we will contact you to obtain your consent. Apart from this we will not continue to contact you

after the completion of the main study, unless there are incidental findings as described above, but you are welcome to contact the university or hospital study office to see if any new information has emerged from subsequent analyses.

Please note that although all identifiers will be removed at this stage a recent study found that a genetic sample cannot be truly anonymized because genetics are individual to a person. Sub-study data will be retained by the investigator for 25 years.

We will not release your identifiable data be released to anyone other than whom you consent to on the final page of this form (i.e. family members, communities, other groups). The only potentially identifiable data that would be released to other trained collaborators/researchers would be your genetic material. This data may also be published in the future in scientific journals or at conferences. At no time would your identifiable information be presented. While we currently have no plans of commercializing (making a profit) any new information that comes from our data, there is a possibility that this may occur.

CAN PARTICIPATION IN THIS SUB-STUDY END EARLY?

Your participation in this sub-study is voluntary and optional and if you choose not to participate, you and your family will continue to have access to customary care at St. Michael's Hospital. You will also be able to continue participating in the main study.

If you choose to withdraw from this long-term storage and/or genetic sub-study, we will retain your serum (blood) and urine samples in the main study for analysis but will destroy your genetic sample and remove your biological samples from long-term storage.

RESEARCH ETHICS BOARD CONTACT

If you have any questions regarding your rights as a research participant, you may contact Dr. David Mazer, Chair, Unity Health Toronto Research Ethics Board (REB) at 416-864-6060 ext. 2557, during business hours.

The Research Ethics Board is a group of scientists, medical staff, and individuals from other backgrounds (including law and ethics) as well as members from the community. The committee is established by the hospital to review studies for their scientific and ethical merit. The Board pays special attention to the potential harms and benefits involved in participation to the research participant, as well as the potential benefit to society. The committee is also required to do periodic review of ongoing research studies. As part of this review, someone may contact you from the Research Ethics Board to discuss your experience in the research sub-study.

STUDY CONTACTS

If you have any questions for the principal investigator, please contact Dr. John Sievenpiper at 416-867-3732 between 9am and 5pm Monday to Friday. Voicemail is available on this phone line. Messages are only picked up by Dr. Sievenpiper.

The sub-study coordinator will be available to answer your questions regarding the sub-study between 9am and 5pm Monday to Friday. Please call the following number to speak to the sub-study coordinator: 416-867-7460 ext. 48216. Voicemail is available on this phone line.

STATEMENT OF INFORMED CONSENT

STOP SUGARS NOW Trial: Genetic Sub-study

The research sub-study has been explained to me, and my questions have been answered to my satisfaction. I have been informed of the alternatives to participation in this sub-study. I have the right not to participate and the right to withdraw without affecting the quality of medical care at St. Michael's Hospital for me and for other members of my family. As well, the potential harms and benefits (if any)

STOP SUGARS NOW Long-Term Banking and Genetic Sub-study

Principal Investigator: Dr. John L Sievenpiper

Version 2: Updated 28-December-2018

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of participating in this research sub-study have been explained to me. I have been told that I have not waived my legal rights nor released the investigators, sponsors, or involved institutions from their legal and professional responsibilities. I know that I may ask now, or in the future, ask any questions I have about the sub-study. I have been told that records relating to me and my care will be kept confidential and that no information will be disclosed without my permission unless required by law. I have been given sufficient time to read the above information.

Please check the box and initial your selection for the <u>optional</u> components of the sub-study:	
<p>Long-term Storage & Future Use for Research of Biological Samples: I hereby consent to my biological (urine, feces, blood) samples being stored for up to 30 years after the end of the main study and for them to be used in relation to the objectives of this research sub-study.</p>	<p>I consent <input type="checkbox"/> _____</p> <p>I do <u>not</u> consent <input type="checkbox"/> _____</p>
<p>Future Use for Research of Genetic Samples: I hereby consent to my genetic samples being stored for up to 30 years after the end of the main study and for it to be used in relation to the objectives of this research sub-study.</p>	<p>I consent <input type="checkbox"/> _____</p> <p>I do <u>not</u> consent <input type="checkbox"/> _____</p>

Findings and notification of family/ primary care physician

In the event that new medical information is detected during the genetics research and the information is determined by investigators to be clinically significant:

- _____ (initials) Yes, I would like to know and want to be informed of this information
- _____ (initials) No, I do not want to be informed of this information

- _____ (initials) Yes, I would like to have this information forwarded to my family doctor.
- _____ (initials) No, I do not want this information forwarded to my family doctor

I consent to participate. I have been told I will be given a signed copy of this consent form.

Name of Participant (Please Print)	Signature of Participant	Date (Day/ Month/ Year)

I confirm that I have explained the nature and purpose of the sub-study to the participant named above. I have answered all questions asked about the sub-study.

Name & Position of Person Conducting Consent Discussion	Signature of Person Conducting Consent Discussion	Date (Date/ Month/ Year)