Official Title: Optimizing Fluoride Retention in the Mouth of Older Adults With Distinct Salivary Flow Rates

NCT Number: NCT04239872

Document Date: 8/24/2022

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: Optimizing fluoride retention in the mouth of older adults with distinct salivary flow rates
Company or agency sponsoring the study: MICHR
Principal Investigator: Livia M. A. Tenuta, DDS, MSc, PhD, Department of Cariology, Restorative Sciences and Endodontics, University of Michigan School of Dentistry
Study coordinator: Taylor M. Cezon, RDH, BSDH, University of Michigan School of Dentistry

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find child care, or make other plans. In your decision to participate in this study, consider all of these matters carefully.

This research is studying a new type of fluoride mouth rinse in small numbers of people to learn about its safety and its effect on your body. This study will assess if rinsing with calcium before rinsing with a fluoride mouth rinse can increase the retention of fluoride in the mouth. In the first research visit, we will check your oral health and measure how much saliva you have in your mouth. In the second research visit, you will be asked to rinse with one of the mouth rinses under test in the study (fluoride only of a calcium rinse followed by a fluoride rinse). Finally, in the third visit, you will be asked to rinse your mouth with the other rinse (not tested before). Your saliva and dental plaque samples will be collected after you do the rinses in visits 2 and 3, for analysis of fluoride concentration.

This study involves a process called randomization. This means that the mouth rinse you will use in the second visit is not chosen by you or the researcher. The study design divides study participants into separate groups, based on chance (like the flip of a coin), to start the study in different treatments. In the third visit, you will use the other treatment. You will know in which group you are in because one of

the treatments involves one mouth rinse, the other involves two mouth rinses. But you will not be able to choose in which treatment to start.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include the discomfort in the collection of saliva or rinsing with the mouth rinses, or discomfort to be asked to come to the School of Dentistry without having brushed your teeth in the morning. More detailed information will be provided later in this document.

This study may offer some benefit to you now or others in the future by developing an improved fluoride rinse to keep fluoride longer in the mouth. More information will be provided later in this document.

We expect the amount of time you will participate in the study will be one month.

You can decide not to be in this study. Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

People with dry mouth tend to have more oral diseases. We know that using fluoride is helpful, but the effect of fluoride has a limit, especially in people with dry mouth. However, a new type of fluoride treatment, associated with calcium, is showing better results than fluoride alone in order to retain fluoride in the mouth. In this study we will test how well this treatment (a mouth rinse with calcium and fluoride) works in older individuals with different rates of production of saliva.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Individuals with at least 65 years of age, who are able to follow the study instructions, who have at least 20 teeth in the mouth, and at least 4 teeth in each side of the upper and lower parts of the mouth.
If you have dental pain or need urgent dental care, you are not eligible to participate.

3.2 How many people are expected to take part in this study?

20 subjects are expected to participate.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

You will have to follow the following instructions during the study:

- Use a standardized toothpaste and toothbrush, provided to you by the study team at your first visit, starting 7 days before your scheduled return for visits 2 and 3. This is to make sure every participant is using the same type of fluoride in the toothpaste.
- Do not rinse your mouth with any other oral product during the study period
- Do not drink green or black tea on the night before or the day of their visits. These teas have a high fluoride content.
- Do not brush your teeth on the night before and the morning of the study visits 2 and 3
- Do not eat or drink for 2 hours after the rinses during visits 2 and 3. Your saliva and plaque will be collected during this period.

You can find details about what will happen during each visit below:

Visit 1 – about an hour

You will be scheduled for a first visit to the School of Dentistry to check your eligibility to participate in this study. In this visit, you will have your teeth examined, and will be asked to collect two samples of saliva, one without stimulation (just drooling into a tube) and the other while chewing gum. The amount of saliva you produce will be used as one of the eligibility criteria. During this visit, we will also ask you to report the list of medications that you regularly take. If you are eligible, you will also receive a standardized toothpaste and toothbrush, which you will have to use for one week before visits 2 and 3.

Visit 2 & 3 – about 3 hours for each

If you are eligible, you will be scheduled to come to the School of Dentistry 2 more times within the next 2 to 4 weeks. These visits will be at least 7 days apart. In Visit 2, you will be randomly assigned to one of two treatments (like flipping a coin). One of the treatments is a mouth rinse with fluoride (one rinse only), the other is a mouth rinse with calcium followed by a mouth rinse with fluoride (2 rinses). If you are assigned to use the one-rinse treatment in visit 2, you will use the 2-rinse treatment in visit 3, and vice versa.

For each visit, you will have to come to the School of Dentistry in the morning, without having brushed your teeth. When you arrive, the study team will ask you to drool saliva into a tube; they will also collect a sample of dental plaque from your teeth. You will then do a mouth rinse with the assigned treatment (only 1 rinse or 2 rinses). Each rinse is done for 1 minute, and then spit out. After rinsing, we will collect 3 more dental plaque samples from your teeth (at 15, 60 and 120 min after the rinse(s)); each collection should be done in one minute. We will also ask you to drool saliva into a tube immediately after collecting the dental plaque sample (at 16, 61 and 121 min after the rinse(s)) and also at time points 30 min and 90 min after the rinse.

As a subject participating in this research study, you have certain responsibilities that may apply to this study, such as ensuring that you arrive in time for all of your scheduled appointments, do your rinse and collect saliva samples as directed, and report any adverse reactions (e.g. feeling your mouth different after the rinses, feeling the taste of food different) you may have during the study.

4.2 How much of my time will be needed to take part in this study?
You will participate in a first visit that will last about 1 hour. The following visits (2 and 3) will last about 3 hours each. At least 7 days will be allowed between visits 2 and 3. Therefore, your total participation in the study is expected to be about one month.

4.3 When will my participation in the study be over?
At the end of visit 3 your participation in the study will be over.

4.4 What will happen with my information and/or biospecimens used in this study?
Your biospecimens and collected information may be shared with MICHR (Michigan Institute for Clinical and Health Research).

With appropriate permissions, your biospecimens and collected information may also be shared with other researchers, here, around the world, and with companies.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?
The known or expected risks are:

- The most common discomfort (occurring in more than 25% of patients) is related to not brushing your teeth the night before and in the morning of visits 2 and 3. You may feel bad breath in the morning of the test due to not brushing. The researchers will try to minimize this discomfort by having you brush your teeth under supervision or performing a professional cleaning at the end of the visit to remove dental plaque.
- Less common discomforts (10% - 25% of patients) are:
    - Discomfort related to collecting saliva samples, as some individuals may not feel comfortable to drool into a tube. This discomfort will be minimized by keeping you seated in a private dental chair, with only the trained study staff offering instructions on the procedure.
    - Discomfort related to rinsing with unflavored rinses. This discomfort will be minimized by having you only rinse for about 1 minute with each rinse.
    - Discomfort related to refraining from eating or drinking for up to 2 hours during the collection of samples. This may be harder if you have dry mouth and sip water constantly. In order to minimize this discomfort, if required, you will be allowed to drink a small amount of water.

Additionally, there may be a risk of loss to confidentiality or privacy. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may not receive any personal benefits from being in this study. However, you will receive oral hygiene and care instructions provided by the study personnel. Also, in case we find out that you have low production of saliva, you will be informed about this, because this condition increases the risk for oral diseases. You may also benefit from the understanding of the study objectives, and by being more motivated for taking care of your oral health.

Even if you do not benefit directly, others may benefit from the knowledge gained from this study.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?
This study is not meant to treat any condition or disease. Even if you have dry mouth, the mouth rinses to be tested are not considered standard of care for the prevention of any oral disease, including tooth decay. You will be provided with all information available about your oral health and where you can find treatment available, shall we find any treatment needs during the study procedures.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information”.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
No, we do not anticipate any harm to you if you leave the study before the end.

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
There are not costs or billing for this study. If you get a bill you think is wrong, call the researcher's telephone number listed in Section 10.1.
By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
Yes, you will receive gift cards that amount to $84 for completing the study. This payment will be prorated; you will receive $18 for completing visit 1, $18 for completing visit 2 and $48 for completing visit 3. If you withdraw from the study you will only be paid up to the point when you withdraw.

The gift cards will be reloaded with the next payment so it is very important that you keep your gift card the whole study.

8.3 Who could profit or financially benefit from the study results?
The American Dental Association Foundation is an owner and Dr. Gerald L. Vogel is a named inventor on patents or patent applications on the use of calcium before a fluoride rinse. This means, the American Dental Association Foundation and Dr. Gerald L. Vogel could gain financially from this study.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?
Your research information will be stored in password-protected electronic files or locked storage cabinets accessible only to the study personnel. Standards for data collection, management and analysis will be followed.

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.

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results and dental records
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, Social Security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities. (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Livia M. A. Tenuta
Mailing Address: 1011 N University Ave, room 2217, 48109, Ann Arbor, MI
Telephone: 734-763-3703

Study Coordinator: Taylor M. Cezon
Mailing Address: 1011 N University Ave, room 3323c, 48109, Ann Arbor, MI
e-mail: thouseho@umich.edu

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies, include the appropriate calling codes.)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document, signed and dated (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Sig-A

Consent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Sig-G

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____