Reducing Sugared Fruit Drinks in Alaska Native Children

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STATEMENT OF COMPLIANCE

The study will be conducted in accordance with the International Council for Harmonisation guidelines for Good Clinical Practice (GCP) (ICH E6) and the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46). National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

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LIST OF ABBREVIATIONS

Ace-K	Acesulfame Potassium
ADI	Acceptable Daily Intake
AE	Adverse Event
AIAN	American Indian Alaska Native
CFR	Code of Federal Regulations
CHW	Community Health Worker
DSMB	Data and Safety Monitoring Board
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GEE	Generalized Estimating Equations
ICH	International Council for Harmonisation
IFC	Intra-Family Correlation
IOM	Institute of Medicine
IRB	Institutional Review Board
NIDCR	National Institute of Dental and Craniofacial Research
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PI	Principal Investigator
PO	Program Official
PPE	Personal Protective Equipment
RCT	Randomized Clinical Trial
SAE	Serious Adverse Event
SD	Standard Deviation
US	United States
UAF	University of Alaska Fairbanks
UW	University of Washington
WHO	World Health Organization
YK	Yukon-Kuskokwim
YKHC	Yukon-Kuskokwim Health Corporation

PROTOCOL SUMMARY

Title: Reducing Sugared Fruit Drinks in Alaska Native Children

Précis: Alaska Native children consume an average of 50 teaspoons of sugar per day and most of this added sugar is from fruit drinks like Tang and Kool-Aid. The goal of this **community-based behavioral trial** is to reduce sugared fruit drink intake in **Alaska Native children**. In Communities A and B, a total of 136 children ages 1-11 years will be recruited for a 6-month culturally-adapted, 5-session intervention consisting of **video-based health education** and **self-efficacy** coaching delivered in person (or via Internet or phone in case of Covid-19 restrictions) by an indigenous **Community Health Worker**. There will be 4 brief "check-ins" to provide social support (delivered via phone or through brief in-person visits outside the home in case of Covid-19 restrictions). Local stores have been recruited to carry sugar-free fruit drinks. In Community C, 56 children will be recruited to a delayed treatment control group. Outcomes will be measured at baseline, 1, 3, 6, and 12 months.

Objectives: The primary child-level outcome: added sugar intake (grams of added sugar/day, measured via hair biomarker). The secondary outcome is caregiver-level added sugar intake (grams of added sugar/day, measured via hair biomarker). Exploratory outcomes include (a) caregiver knowledge, beliefs, and self-efficacy (measured via the fruit drink survey) and (b) sales of the sugar-free water enhancers (measured via sales reports from stores).

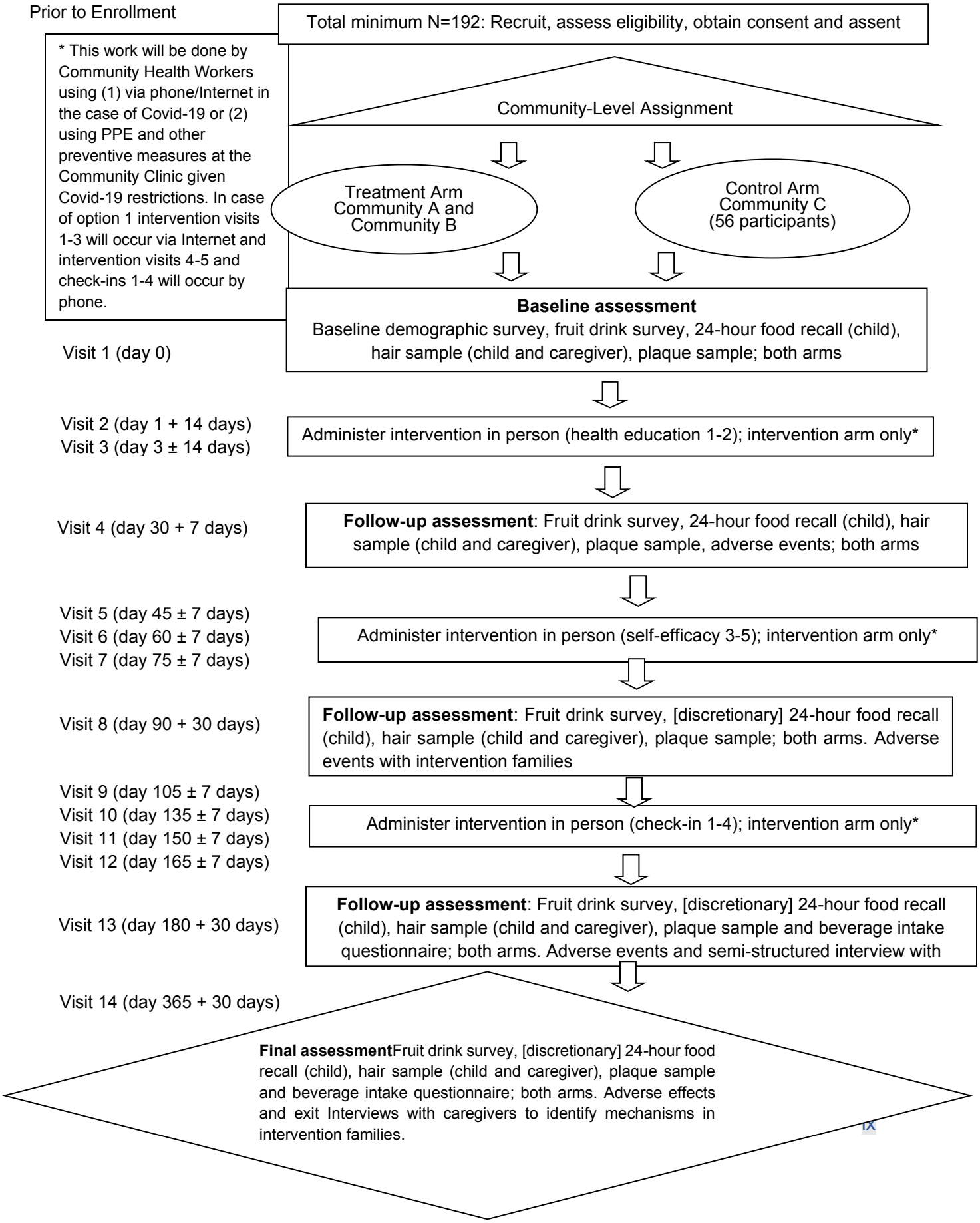
The primary objective is to test the hypothesis that children in the intervention arm will have lower sugar intake compared to children in the no-treatment control arm.

The secondary objective is to compare differences in added sugar intake associated with the proposed intervention in caregivers.

There are four exploratory objectives: 1) to identify potential mechanisms associated with changes in sugared fruit drink and added sugar intake, 2) to assess sales of the sugar-free water enhancers, 3) to investigate how diet contributes to added sugar intake among child participants, and 4) to assess potential changes in mutans streptococci levels associated with the intervention.

Population:	192 Alaska Native caregivers and their children ages 1-11 years who live in one of three YK Delta study communities.
Phase or Stage:	Phase II
Number of Sites:	3 Alaska Native communities
Description of Intervention:	Children and their caregiver(s) in the intervention communities will receive a culturally-adapted, 5-session program consisting of video-based health education and self-efficacy coaching delivered by an indigenous Community Health Worker. Families will be introduced to sugar-free water enhancers that are commercially available and come in the same flavors as regular Tang and Kool-Aid. The sessions will include conversations on related topics, interactive hands-on activities, and homework assignments. Additionally, four brief "check-ins" will keep families engaged. Local stores in the intervention communities only will carry the sugar-free water enhancers that are highlighted in the health education. The delayed intervention for the control group will consist of the option to receive the home-based or remote-visits consisting of health education, self-efficacy coaching, and check-ins after the last data collection visit at 12 months.
Study Duration:	2 years (from enrollment to data analysis and publication)
Subject Participation Duration:	1 year
Estimated Time to Complete Enrollment:	1 month

SCHEMATIC OF STUDY DESIGN


Prior to Enrollment
Total minimum N=192: Recruit, assess eligibility, obtain consent and assent
* This work will be done by Community Health Workers using (1) via phone/Internet in the case of Covid-19 or (2) using PPE and other preventive measures at the Community Clinic given Covid-19 restrictions. In case of option 1 intervention visits 1-3 will occur via Internet and intervention visits 4-5 and check-ins 1-4 will occur by phone.
Community-Level Assignment
Treatment Arm Community A and Community B
Control Arm Community C (56 participants)
Visit 1 (day 0)
Baseline assessment
Baseline demographic survey, fruit drink survey, 24-hour food recall (child), hair sample (child and caregiver), plaque sample; both arms
Visit 2 (day 1 + 14 days)
Visit 3 (day 3 ± 14 days)
Administer intervention in person (health education 1-2); intervention arm only*
Visit 4 (day 30 + 7 days)
Follow-up assessment: Fruit drink survey, 24-hour food recall (child), hair sample (child and caregiver), plaque sample, adverse events; both arms
Visit 5 (day 45 ± 7 days)
Visit 6 (day 60 ± 7 days)
Visit 7 (day 75 ± 7 days)
Administer intervention in person (self-efficacy 3-5); intervention arm only*
Visit 8 (day 90 + 30 days)
Follow-up assessment: Fruit drink survey, [discretionary] 24-hour food recall (child), hair sample (child and caregiver), plaque sample; both arms. Adverse events with intervention families
Visit 9 (day 105 ± 7 days)
Visit 10 (day 135 ± 7 days)
Visit 11 (day 150 ± 7 days)
Visit 12 (day 165 ± 7 days)
Administer intervention in person (check-in 1-4); intervention arm only*
Visit 13 (day 180 + 30 days)
Follow-up assessment: Fruit drink survey, [discretionary] 24-hour food recall (child), hair sample (child and caregiver), plaque sample and beverage intake questionnaire; both arms. Adverse events and semi-structured interview with
Visit 14 (day 365 + 30 days)
Final assessmentFruit drink survey, [discretionary] 24-hour food recall (child), hair sample (child and caregiver), plaque sample and beverage intake questionnaire; both arms. Adverse effects and exit Interviews with caregivers to identify mechanisms in intervention families.

KEY ROLES AND CONTACT INFORMATION

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INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

1.1 Background Information

Tooth decay is a major public health problem in American Indian and Alaska Native (AIAN) children (Batliner et al. 2014; Chi et al. 2015). An important risk factor for tooth decay is added sugar intake (Sheiham and James 2014). Added sugars are defined as sugars used as ingredients in prepared or processed foods and sugars eaten separately or added to foods. Sucrose and high fructose corn syrup are the most common added sugars in the U.S. (Vos et al. 2017). The American Heart Association recommends that children under age 2 years should avoid consuming any added sugar and children ages 2 to 17 years should consume no more than 6 teaspoons of added sugar per day (Vos et al. 2017).

Pre-R56 Pilot Research

In Alaska's Yukon-Kuskokwim (YK) Delta, most added sugar is from sugared fruit drinks, like Tang and Kool-Aid (Chi et al. 2015). Preliminary research with 54 Yup'ik Alaska Native children ages 6 to 17 years showed that participants consumed an average of 50 teaspoons of added sugar/day, 8 times the American Heart Association's recommended maximum (Chi et al. 2015). Added sugar was measured using a validated hair biomarker (Nash et al. 2014). The data also confirmed a statistically significant relationship between added sugar and tooth decay, underscoring the potential to reduce tooth decay prevalence by addressing sugared fruit drink intake.

Community members in the YK Delta expressed concerns about the health consequences of sugared fruit drinks like Tang and Kool-Aid. They noted that most Yup'ik caregivers: (1) do not know about the high sugar content of Tang and Kool-Aid; (2) would be willing to try sugar-free alternatives; and (3) need the sugar-free alternatives to be available locally to help support the switch away from Tang and Kool-Aid. Community members knew that water and milk were ideal beverages but did not believe an intervention focusing on water or milk would be successful because most Yup'ik children have already developed a taste for sugared fruit drinks. All interviewed community members were unaware that the same companies that make Tang and Kool-Aid also make sugar-free versions of these drinks that come in the same flavors. These are called sugar-free water enhancers. They are commercially available drops containing sugar-free sweeteners, like sucralose and acesulfame potassium, and flavoring. The drops are added to drinking water to make the water taste like regular versions of drinks like Tang and Kool-Aid, but do not contain any sugar. Members tried the proposed sugar-free water enhancers, which are almost identical to the sugared versions. They believed the sugar-free water enhancers were easy to use, liked the flavors, and reported their children would like them too.

Community members also expressed the strengths of having an indigenous member of the community to deliver the intervention rather than having an outsider. This person would know about the history of the YK Delta, have at least some working knowledge of Yup'ik culture, and at least understand some of the Yup'ik traditions. It would be important to make sure the selected interventionist is a respected member of the

community. An added benefit is that the job would provide some external income and perhaps some future career opportunities for the selected interventionists. For these reasons, we decided that the interventionists would be recruited from within the study communities and trained on how to deliver the intervention components.

R56 Funded Research

To confirm caregiver reports that Yup'ik children would like the sugar-free water enhancers, taste tests were conducted with 89 Yup'ik children ages 7 to 10 years in Bethel (Chi et al. 2019). There was no difference in preference for the sugared fruit drinks versus the sugar-free water enhancers for all 4 flavors that were evaluated (Tang, Kool-Aid Grape, Kool-Aid Tropical Punch, Kool-Aid Cherry).

1.1.1 Rationale

There is an unresolved childhood tooth decay epidemic in indigenous communities, driven largely by intake of large amounts of added sugars, and a desire on the part of study communities to begin addressing the problem. The proposed study will begin addressing this epidemic by evaluating a behavioral intervention that was developed with critical and ongoing input from caregivers in local YK Delta communities. The intervention will educate caregivers about the harmful effects of sugared fruit drinks, empower caregivers to make healthier beverage decisions by adopting sugar-free water enhancers for their children, provide ongoing social support, and give families a place to obtain and purchase sugar-free water enhancers.

The rationale for the study is the dearth of research on community-based behavioral programs focusing on improving oral health behaviors in indigenous populations. The work is expected to benefit the study communities and other vulnerable communities that face similar types of problems caused by added sugar intake.

The main study hypothesis is that children in the intervention arm will have lower sugared fruit drink intake and added sugar intake compared to children in the no-treatment control arm.

1.2 Potential Risks and Benefits

1.2.1 Potential Risks

Potential risks for dignitary harm and lack of respect. To offset this concern, the study staff members will obtain the informed consent of participants electronically via laptops in a respectful, dignified manner following guidelines in place for the protection of human participants. In case of Covid-19 restrictions, informed consent may be conducted remotely by sending a REDCap link to the participant for their signature and conducting informed consent via phone. All oversight bodies (YKHC Human Studies Committee, Tribal Councils) will review cultural appropriateness of the consent process.

Potential risk for psychological distress. There is a low risk of psychological distress associated with participating in this study. Questions related to the child's sugared fruit drink consumption may cause embarrassment, anxiety, or discomfort for some caregivers. Study participants will be advised of this risk during the informed consent process and allowed to discontinue participation in the study at any time with no negative repercussions, including no loss of health benefits to which they are entitled through the YKHC. All the hair samples collected for the study are destroyed during processing and there is no leftover hair for banking. There will be no testing for drugs or other substances on the hair specimens collected for this study. Plaque samples will be banked and eventually analyzed to see if the intervention affected the concentration and makeup of bacteria in the mouth. Plaque samples will be destroyed by the end of the study period in full and ongoing consultation with YKHC.

Potential risk for loss of confidentiality. The communities are small, which makes it likely that community members will know who is participating in the study. Community Health Workers have completed human subjects training and will ensure that all interactions with families are kept confidential and that data are protected. In light of this, protocols will ensure that there are no identifiers on data collection documents and that all documents are stored securely. Paper documents will be stored in locked cases. Electronic data will be stored on password-protected, encrypted computers.

Potential risk for psychological, social, cultural, and dignitary harm in communities. One potential risk is internal stigmatization (or "self-stigmatization"). For instance, if negative results are released to the public in a potentially stigmatizing manner, both participants and nonparticipating residents may self-stigmatize (i.e., consider themselves to be "defective" or "bad" or to have similar negative attributes). External stigmatization (i.e., stigmatization by outsider people against identified subgroups or the entire community), may also occur. We will ensure that all dissemination of findings is done respectfully, without blaming communities or families. Study communities will not be identified by name and only by letters (A, B, and C) in all publications and presentations.

Potential excess intake of sugar-free sweeteners. The target sugar-free water enhancers are commercially available. They contain sucralose and acesulfame potassium (ace-K), both of which are artificial sweeteners that are well-established as safe, based on extensive toxicological safety data submitted to the U.S. FDA and other regulatory agencies worldwide (IOM 2002/2005; Magnuson et al. 2017; Magnuson et al. 2016; Sylvetsky and Rother 2018; Sylvetsky et al. 2017). Side effects of too much intake of the sugar-free drinks include stomach ache and diarrhea. The side effects resolve without treatment when the individual stops consuming the sweetener.

There are multiple strategies the study will employ to protect study participants and make sure they stay within the safe limits of sugar-free water enhancer intake. These are detailed in our Data and Safety Monitoring Plan. See Section 9.1 for safety parameters.

First, the health education part of the intervention emphasizes plain water and milk as the healthiest beverages for children, especially for children age 3 years and younger.

Second, the health education will include information about potential side effects and the importance of limiting intake of the sugar-free drinks. Caregivers will be instructed to allow only adults to mix the drinks and to store the sugar-free water enhancers out of reach of children.

Third, health education materials will recommend diluting the sugar-free water enhancers and following instructions on maximum numbers of servings per day that are provided to caregivers on a laminated card. CHWs will reinforce these instructions.

Fourth, CHWs and study staff will monitor for side effects throughout the study. Local health aides, who are trained medical health providers employed by YKHC and live and work in the study communities, will be educated about the intervention and trained to identify side effects (see Manual of Procedures).

1.2.2 Potential Benefits

There are no known benefits to study participants. If the intervention is efficacious, potential health benefits to the study participants include increased knowledge about the harmful health effects of sugared fruit drinks and reductions in added sugar intake. In the long-term, there could be societal benefits in the form of reduced risk of diseases like tooth decay, obesity, and other chronic diseases linked to sugar sweetened beverages. The study is expected to generate new knowledge that can be used in the future to improve health and well-being of Alaska Native children and other vulnerable communities in which sugared fruit drinks are pervasive.

OBJECTIVES AND OUTCOME MEASURES

2.1 Primary

Objective	Brief Description/Justification of Outcome Measure	Outcome Measured By	Time Frame
The primary objective is to test the hypothesis that children in the intervention arm will have lower added sugar intake compared to children in the no-treatment control arm.	The primary child level outcome is added sugar intake (grams of added sugar/day). This outcome is the main target of the intervention because added sugar intake is a primary determinant of tooth decay for children in the study communities.	Added sugar intake will be measured with a validated hair biomarker that will be obtained by trained UW study staff. In case of Covid-19 restrictions, hair samples may be self-collected by participants. If done in person, we will protect participants and staff with PPE and other precautions consistent with local and UW policies (e.g., vaccination, shields).	Baseline to 6 months.

2.2 Secondary

Objective	Brief Description/ Justification of Outcome Measure	Outcome Measured By	Time Frame
To compare differences in added sugar intake associated with proposed intervention in caregivers.	Caregiver-level added sugar intake (grams of added sugar/day). The intervention is expected to decrease the amount of added sugars consumed by caregivers in the intervention communities. An alternative hypothesis is no difference because the intervention specifically targets child intake and not caregivers.	Validated hair biomarker. Obtained by trained UW study staff. In case of Covid-19 restrictions, hair samples may be self-collected by participants or collected in person using precautions.	Baseline to 6 months.

2.3 Exploratory

Objective	Brief Description/Justification of Outcome Measure	Outcome Measured By	Time Frame
To identify potential mechanisms associated with changes in sugared fruit drink and added sugar intake.	Behavioral survey questions to assess changes in caregiver knowledge, beliefs, and self-efficacy (see Manual of Procedures). The intervention is expected to change some of these behavioral factors, which could explain why the intervention works for some and not others.	Fruit drink survey completed by caregiver (one for each child). Obtained by trained UW study staff. In case of Covid-19 restrictions, the fruit drink survey may be conducted via phone by UW study staff or collected in person using precautions.	Baseline to 6 months.
To investigate how diet contributes to added sugar intake among child participants.	24 hour food recall data will be used to assess sugared fruit drink intake and to identify other dietary factors related to the primary outcome, added sugar intake.	Sugared fruit drink and food intake will be measured through 24 hour dietary recall interviews with caregivers, for each child at baseline and 1-month; a validated dietary intake measure using the Nutrition Data System for Research (NDSR).	Baseline, 1 month
To test the hypothesis that children in the intervention arm will have lower sugar fruit drink consumption after receiving the intervention, compared to children in the no-treatment control arm.	Beverage intake questionnaires will be used to assess sugared fruit drink intake (servings per day) among child participants.	Sugared fruit drink intake will be measured using validated beverage intake questionnaires (BEVQ-15) at 6-months and 12-months; which will be administered to caregivers to provide responses, for each child.	6 months and 12 months

Objective	Brief Description/Justification of Outcome Measure	Outcome Measured By	Time Frame
To assess for potential changes in mutans streptococci levels associated with the intervention.	Changes in mutans streptococci levels and oral microbiome features will be measured through analysis of oral plaque samples collected from children enrolled in the study.	A measure of mutans streptococci level will provide a proxy for microbiological changes associated with changes in sugared fruit drink and added sugar intake.	Baseline, 1 month, 3 months, 6 months and 12 months. Samples will be banked and securely stored until there is funding for these analyses.

STUDY DESIGN

This is a 2-arm community-based behavioral trial. Participants, interventionists, investigators, and outcomes data collection staff will not be masked because it is not feasible. Data processors will be masked. While attempts will be made to mask the analyst, it will likely not be effective because of the different sizes of the intervention and control groups.

There is a total of 3 study communities (2 in the intervention arm and 1 in the no-treatment control arm). The 3 communities are located in Alaska's YK Delta, about an hour by airplane from Bethel. The 2 communities in the intervention arm are about 15-minutes away from each other by airplane. The community in the control arm is about 45 minutes away from the 2 communities in the intervention arm, which will help to minimize contamination between the control and the 2 treatment arms.

Two communities will be in the intervention arm and one community in the control arm. Allocation to the intervention arm was based on the order in which communities were ready to participate in the study as assessed during recruitment of communities. Randomizing at the community-level would have required a sample size that is beyond the scope of the current study budget. Randomizing at the family- or child-levels would not have been possible because of the small size of study communities and high risk of contamination between families or among children from the same family.

The focus is on Yup'ik Alaska Native communities because of the high rates of added sugar intake and tooth decay. Children are the focus of the primary outcome measure based on the potential for a lifetime of benefit associated with reduced added sugar intake. Outcomes will also be measured at the caregiver and community levels.

Enrollment is expected to take 1 month. Study participation will last 1 year.

There are 2 arms: an intervention arm and a control arm. 136 children in Communities A and B will be assigned to the intervention arm (in-person video-based health education led by a Community Health Worker, self-efficacy coaching, brief "check-ins", access to stores that sell the target sugar-free water enhancers). In case of Covid-19 restrictions the health education and self-efficacy coaching may be delivered via phone or Internet video and the check-ins via phone, video call, or in-person outside the home. There will be a total of 5 visits and 4 brief "check-ins" (total face time of 2-3 hours). This visit frequency was determined as acceptable by community members in terms of being sufficient time to educate caregivers and motivate behavior change without overburdening families. Indigenous Community Health Workers who are from and live in the study communities will deliver all intervention components to maximize cultural saliency.

56 children in Community C will be assigned to the delayed treatment control arm. Children in the control arm will have the opportunity to receive similar intervention components after the study ends, that incorporates learned lessons from the

intervention to improve content and delivery. If Covid-19 continues to result in restrictions at the end of the study Community C participants may also receive virtual visits by phone or Internet video. This will involve CHW or UW study staff-delivered health education, self-efficacy training, and check-ins. We will provide families with an equivalent number of sugar-free water enhancers distributed during the second health education visit for the intervention communities, based on household size. We will work with stores to start selling sugar-free water enhancers from the start of the control community intervention throughout the 6-months. We will also inform stores that there may be increased demand for these sugar-free water enhancers and provide them with ordering information. The control community intervention however, will last only 3 months, one-half of the time over which families in Communities A and B will have received the intervention. We will evaluate outcomes for control families for as long as the budget will allow.

The main outcome is added sugar intake in children in 3 Yup'ik communities (change from baseline to 6 months). The outcome will be measured at baseline, 1, 3, 6, and 12 months. Data will be collected in person and involves collecting a hair sample from child participants (from which added sugar will be measured using a validated biomarker) (see Manual of Procedures). Hair samples will be processed at UAF. All other data will be managed at UW. As noted, in case of Covid-19 restrictions, hair samples may be self-collected by participants. See instructions for self-collection of hair samples in Appendix M.

3.1 Sub Studies

There is 1 proposed sub-study in which plaque samples will be collected from participants at each data collection visit (see Manual of Procedures). Plaque specimen collection will be required. The plaque samples will be banked at UW and then analyzed in the future to assess for potential changes in mutans streptococci levels and other bacteria in the mouth associated with the intervention using microbiome techniques. The rationale is that the study lacks a disease outcome measure in this trial. The intervention lasts 6 months and data collection ends at 1 year, which is not long enough to see changes in tooth decay. A measure of intraoral bacteria levels will provide a proxy for microbiological changes associated with changes in sugared fruit drink and added sugar intake. The samples will be stored according to the specimen kit manufacturer instructions at the UW School of Dentistry and non-study staff will not have access to the samples. The samples will be labeled with a de-identified study ID. The consent form will include an additional line for participants to consent to plaque sample banking and analyses. The samples will be destroyed by the end of 2027, and will be done in close consultation with the YKHC. In case of Covid-19 restrictions, the plaque samples may not be collected, as they require in-person contact with a UW staff person and thus travel to the region, but in-person collection may be possible with added Covid-19 precautions.

STUDY POPULATION

4.1 Participant Inclusion Criteria

To be eligible to participate in this study, an individual must meet all of the following criteria:

- Child must be older than age 1 year but less than age 12 years at time of enrollment. Multiple children from the same family are eligible;
- Child must live in one of the study communities;
- Child's parent or primary caregiver must of Yup'ik descent, be age 18 years or older, and willing to provide written consent to study procedures;
- Child participant(s) ages 8 to 11 years must be willing to provide written assent to study procedures. Age 8 is the minimum age at which the UW IRB requires assent;
- Willing to comply with all study procedures and be available for the duration of the study.

4.2 Participant Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

- Severe medical condition that would prevent them from completing the study procedures;
- Allergy to sucralose or acesulfame potassium (sweeteners in the sugar-free water enhancers) as defined by parent report of any known allergies;
- Sulfa drug allergy (potential hypersensitivity to acesulfame potassium)
- Member of the same household as the Community Health Worker who will be delivering the intervention.

4.3 Strategies for Recruitment and Retention

We will work with YKHC and may send mailings to all families in the 3 study communities. These mailings will be placed in their local postal boxes and will have information about the study, links to the study website, how to enroll, and dates of enrollment. We will also use contact information obtained from participants in the pre-intervention hair study and get in touch with families who expressed an interest in participating in future studies. All families who participated in the pre-intervention hair study will also be sent findings from the hair study, which will serve the purpose of

disseminating findings but also to give interested families the chance to enroll for the full intervention through the study website.

The enrollment goal is 192 Yup'ik children ages 1 to 11 years from the 3 study communities. About 410 children in the target age range who reside in the 3 study communities will be screened to reach the enrollment goal.

To ensure that all eligible families are reached and that the target enrollment goal is met, advertisements for the study will be placed on a study website, Facebook, community bulletin boards, local VHF radio, washeteria boards, and word-of-mouth.

Stores in the 2 intervention communities (A and B) have already been recruited as sites where caregivers will be able to obtain sugar-free water enhancers (see Manual of Procedures).

The intervention was designed for younger children because they are more likely than older children to drink Tang and Kool-Aid and most will still have primary teeth. This is why children older than age 11 years are excluded at baseline. The study focuses on Yup'ik Alaska Native children, which is appropriate because almost everyone living the study communities is of Yup'ik descent. Safeguards are in place to prevent coercion by requiring caregiver consent from all child participants and assent from children age 8 years and older.

Participating caregivers will receive a $25 gift card to the local store for each data collection visit for each participating child. There will be a $50 bonus gift card if the caregiver participates in all 5 data visits (maximum total per child is $175). After the main study period, caregivers from the control group who agree to continue participating will receive a $50 gift card for each data collection visit for each participating child. Families in the two intervention communities will receive free samples of sugar-free water enhancers and vouchers that can be redeemed at the store. Vouchers will not be used in the control community intervention. During the data visits, children will receive a small gift (backpack, water bottle with study logo, study t-shirt, colorful cups, crazy straws). Families and children will also receive fluoride toothpaste and toothbrushes at each visit. In case of Covid-19 restrictions, all these items may be mailed to families instead of providing them in person. Additional retention strategies include maintaining contact with families between visits by creating a closed Facebook page, sending the children birthday cards, and texting and Facebook messaging families visit reminders, which is possible because nearly all families own a cell phone and use texting and Facebook as ways to communicate (see Manual of Procedures).

To minimize loss to follow-up and missing data, attempts will be made to contact participants by phone before all study visits. Often times, it is possible to contact difficult-to-reach individuals in the YK Delta by contacting a close relative, friend, or neighbor – for instance, if a cell phone has become temporarily disconnected. The data collected at baseline will include contact information of a close relative, friend, or neighbor who the study team is given permission to contact in the event a participating

caregiver cannot be contacted. Up to a 7-day period window will be allowed for data collection visit 1 and a 1-month-period for each subsequent data collection visit until an individual is considered to have missing data for that particular visit. An individual will be considered lost to follow-up if he or she fails to return for 3 consecutive data collection visits and is unable to be contacted by the study staff during the times at which the staff are in the communities for data collection.

4.4 Treatment Assignment Procedures

Children in Communities A and B will be assigned to the intervention arm. Communities A and B are the first 2 communities that were recruited to be part of the study. Children in Community C will be assigned to the no-treatment control arm. Community C is the third community that was recruited to be part of the study. The study team made treatment assignment determinations as communities were recruited for the study.

4.4.1 Randomization Procedures (if applicable)

Not applicable.

4.4.2 Masking Procedures (if applicable)

All raw data provided to the statistician will include a participant-level variable indicating the community in which they live. No community names will be included in an attempt to mask treatment assignment.

4.5 Participant Withdrawal or Discontinuation from Study Procedures/Intervention

All study participants are free to withdraw or discontinue from study procedures or the intervention. The power calculations account for 15% to 25% participant attrition, though the actual attrition rate is expected to be much lower based on previous studies in the YK Delta that have had attrition as low as 3%.

4.5.1 Reasons for Participant Withdrawal or Discontinuation from Study Procedures/Intervention

Participants are free to withdraw from the study at any time upon request.

Participants may choose to discontinue the intervention but will continue to be followed unless they choose to withdraw from the study.

An investigator may discontinue an individual's participation in an intervention or withdraw an individual from the study if:

- Any adverse event (AE), defined as an unexpected event associated with the intervention, occurs such that continued participation in the study would not be in the best interest of the participant.

- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.

4.5.2 Handling of Participant Withdrawals from Study or Participant Discontinuation of Study Intervention

For participants who chose to withdraw from the study, or participants who chose to discontinue the study intervention, attempts will be made to collect the reason why. The reasons stated will be documented along with the date on which the participant withdrew or discontinued. Data collection will continue for participants who chose to discontinue the study intervention but chose not to be officially withdrawn (i.e., they would be willing to participate in data collection, but not the intervention). The study will not replace lost or withdrawn participants.

4.6 Premature Termination or Suspension of Study

This study may be suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the investigator or NIDCR. The principal investigator will also promptly inform the IRB and NIDCR and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants.
- Insufficient adherence to protocol requirements.
- Data that are not sufficiently complete and/or evaluable.
- Determination of futility.

STUDY INTERVENTION

5.1 Study Behavioral Intervention Description

The intervention will take place in 3 communities in the YK Delta (not named to keep communities anonymous). Two of the 3 study communities have been assigned to the intervention arm and the third community has been assigned to the control arm. Assignment was based on the order in which communities were recruited for the study. Families in the intervention arm will receive 5 home-based visits. The first 2 visits will consist of video-based health education delivered by an indigenous Community Health Worker that is expected to address knowledge gaps and to introduce families to the sugar-free water enhancers. The remaining 3 visits will focus on self-efficacy coaching to empower caregivers to make the switch to healthier beverages by working with caregivers to identify and help them overcome barriers to behavior change. In addition, there will be 4 brief “check-ins” to keep families engaged in the program. Trained indigenous Community Health Workers (CHW) who live in and are from the study communities will deliver the intervention in person. Stores in the 2 intervention communities have agreed to stock the sugar-free water enhancers that are highlighted in the health education. This intervention by CHWs will be implemented either 1) entirely virtually via phone/Internet in the case of Covid-19 or 2) using PPE and other preventive measures at the local clinic. In case of option 1 intervention visits 1-3 will occur via Internet and intervention visits 4-5 and check-ins 1-4 will occur by phone.

Children in the control arm will receive no treatment initially, but families will have the option to receive the intervention consisting of health education, self-efficacy coaching, and check-ins after the last data collection visit. The same alternative approaches to the intervention will be put in place for the control arm if Covid-19 restrictions are still in place.

Children in the intervention arm will receive a 6-month, 5-session intervention consisting of active video-based health education centered on sugar intake. Two visits will consist of health education, in which families will be shown a short whiteboard video on sugar, tooth decay, and sugar-free alternatives. The video will be interspersed with interactive activities like conversations, games, and hands-on exercises. Three visits are intended to help boost the self-efficacy of caregivers and provide social support. These sessions will focus on discussing barriers to switching to sugar-free water enhancers and ways to overcome these barriers. The last 4 visits will be brief “check-ins” (<5 minutes) to maintain contact with families, provide social support, provide vouchers for sugar-free water enhancers, and encourage sustained behavior change.

All sessions will be delivered in person by an indigenous Community Health Worker who works and lives in the study community, unless alternative approaches are put in place due to Covid-19 restrictions (see above). The intervention visits are expected to

last a total of 2 to 3 hours spread out over 9 visits, which is sufficient to deliver key health education points, build rapport with families, and provide caregivers with long-term support to facilitate behavior change – all while minimizing participant burden (see Manual of Procedures).

There are 3 components to the community-based behavioral intervention: (1) health education; (2) access to alternatives; and (3) self-efficacy coaching and social support.

- **Health education** will address knowledge gaps, reinforce susceptibility to and severity of tooth decay, address normative beliefs about sugared fruit drinks and tooth decay, and highlight the benefits and availability of sugar-free water enhancers. Health education will be the primary focus of the first and second sessions (visits 1 and 2).

- **Local access to alternatives** for families will be assured through the store-based component that is based on the Healthy Stores Program (Gittelsohn et al. 2012). The main stores in the intervention communities have agreed to participate as study partners by making shelf space to sell the sugar-free water enhancers, to accept study vouchers, to track sales, and provide sales data to the study for analyses. We will incentivize stores with a start-up supply of target sugar-free water enhancers.

- **Self-efficacy coaching and social support**. Self-efficacy coaching and social support will be focus of the remaining sessions (visits 3, 4, and 5) as well as the 4 brief “check-ins”. The main activity will involve anticipating and addressing barriers to behavior change – with an emphasis on anticipated and unanticipated barriers. Following health education and the availability of sugar-free alternatives, many caregivers will be excited about making the switch. However, few are likely to anticipate barriers to change, especially on the part of the children and other family members. In Yup’ik culture, the child makes health and dietary decisions, which disempowers caregivers from reinforcing changes. Thus, self-efficacy coaching and social support are meant to help caregivers anticipate barriers so that caregivers are prepared to prevent and address barriers. Part of this will include homework assignments in between visits to anticipate barriers to switching from sugared fruit drink to the sugar-free water enhancers and to work with the CHW to address barriers. These homework assignments will allow caregivers and CHWs to discuss barriers in a non-threatening, supportive way. Samples and vouchers for free sugar-free water enhancers redeemable at the main store in the communities will further reinforce self-efficacy through facilitation and incentive motivation. The brief “check-ins” will help keep families engaged in the program and enthusiastic about behavior change.

Children in the control arm will receive no treatment during the intervention, but will have the option to receive a modified intervention at the end of the study. Modifications will be based on feedback provided from families in the intervention arm. The control community intervention will last 3 months and consist of the same two health education

visits first, in person. Then, the control community intervention participants will have two self-efficacy visits and two check-in visits before the 3 month data collection study visit – all of which will occur remotely by phone, Zoom, and/or text. There will be two data collection study visits at 3 months and 6 months. Vouchers redeemable for sugar-free water enhancers will not be used for the control community intervention.

5.2 Administration of Intervention

A trained and certified indigenous CHWs will deliver health education and self-efficacy coaching to intervention families (see Manual of Procedures) at the local community clinic (or other accessible community space), unless alternative approaches are used due to Covid-19 restrictions (see above). The CHWs will undergo multiple in-person and teleconference-based training sessions to ensure that they know how to deliver the standardized intervention components to study families. We will use checklists to evaluate CHWs as they practice with each other, study staff, and pilot families in the study communities. Each step will involve formal evaluation of CHWs and assessments of performance. There are 3 levels of certification (see Manual of Procedures) and CHWs will be required to meet the highest level of certification before delivering the intervention for the study. During the initial stages of the study, we will evaluate CHWs using checklists to verify that all intervention components are delivered correctly, and retraining will be provided as needed. After this period, the CHWs will use checklists to verify that intervention components were delivered. CHWs will keep careful post-visit field notes on a study visit template to describe each visit with families and explain if particular components were not delivered and why, as applicable. Study staff will review field notes with CHWs to help improve intervention delivery and record keeping. UW study staff may deliver the health education in person, the self-efficacy intervention visits and check-in visits if a CHW is not available in the control community. For families, in the delayed treatment control group, study visits and check-ins may also take place by phone, Zoom, or text message.

5.3 Procedures for Training Interventionists and Monitoring Intervention Fidelity

Co-Investigators and UW study staff will train and supervise the Community Health Workers. Training will consist of in-person training sessions, follow-up sessions by telephone and FaceTime, practice delivery of the intervention with pilot families in the study communities, and additional training sessions by telephone, FaceTime, and in-person if it safe to do so (see Manual of Procedures). The pilot families will be recruited from the communities, with the requirement being that there are no children in the home who would be eligible for the final intervention.

There are 4 levels of certification: initial, intermediate, advanced, and final. To be fully certified, a Community Health Worker needs to achieve final certification. Community Health Workers will deliver health education using a video that will present basic health education and prompt discussions. Scripts and checklists are used to maintain fidelity (see Manual of Procedures). The initial certification will take place after a 2-day, in-

person training in Bethel. The intermediate certification will take place after the Community Health Worker has delivered the first 3 visits to 2 families as part of the pilot intervention. The advanced certification will take place after follow-up trainings on advanced topics in person, by telephone, and by FaceTime with study staff (see Manual of Procedures). The final certification will occur during a 2-day in-person training in Bethel, about three weeks prior to study launch, when CHWs will be asked to demonstrate competency in delivering all components of the intervention visits. Following final certification, mock intervention activities, check-in's and skills assessments will occur via video or phone calls with a co-investigator leading up to study launch (see *final training log* in essential documents).

At the start of the intervention, UW study staff (led by Co-Investigators and Research Coordinators who were part of the CHW training) will accompany Community Health Workers and assess delivery of the intervention via direct observation and checklists and provide feedback after each session. In case of Covid-19 restrictions, this observation will occur via video, with a UW staff person observing the entire session that takes place remotely between the CHW and participating family. A CHW will be considered ready to deliver the intervention independently once they achieve at least 95% on the fidelity checklist with 10 families (see Manual of Procedures). If 95% fidelity is not achieved, the CHW will undergo additional training with study staff and have opportunities to deliver the intervention under supervision. If the CHW is not able to achieve 95% on the fidelity checklist with 5 consecutive families after additional training, they will be replaced.

As part of the ongoing intervention fidelity monitoring, each CHW will keep detailed post-visit field notes using a structured visit form (see Appendix C). These notes will include a checklist of any distractions in the home, intervention components that were delivered, intervention components that were modified or not delivered (along with reasons), follow up items (e.g., get the family a particular flavor sample), and additional notes that will help the CHW deliver subsequent intervention components. These field notes will be completed by CHWs immediately after each visit with a family on a paper form, then scanned and emailed to UW so they can be reviewed by UW study staff remotely. Field notes will be reviewed and phone meetings will be arranged with CHWs to discuss field note contents, challenges, and solutions. In the case of Covid-19 restrictions, the structured visit form will be completed by the CHW in REDCap, where UW staff will review it. In case of Internet connectivity difficulties the CHW will fill in the paper form and then scan and email the form to UW.

For the control community, UW study staff will be trained by the co-investigator who was in charge of training the CHWs. The goal will be for UW study staff to achieve advanced and final certification in order to deliver the intervention components, in lieu of a CHW if they are not available. Fidelity monitoring benchmarks and requirements for ongoing monitoring (i.e., field notes) will be consistent for UW study staff and CHWs.

5.4 Assessment of Participant Compliance with Study Intervention

CHWs will complete field notes after each study visit to record any anomalies related to participant compliance with the study intervention (e.g., home was too loud, caregiver appeared distracted, children were not present), components that were delivered as intended, unanticipated modifications (e.g., parts that were changed or not delivered), and reasons for the modifications. The structured visit form will be completed by the CHW immediately after each visit. The paper form will be scanned and emailed so that UW study staff can monitor them monthly. Phone calls with CHWs will be scheduled as needed to obtain more information, help problem solve, and ensure fidelity with study protocols. If necessary, study staff will travel to the study communities to work with CHWs to help solve any unanticipated problems with intervention delivery. As noted, in case of Covid-19 restrictions, this process will occur in REDCap and no travel to the study communities by UW staff will take place. If the control community intervention is delivered by UW study staff, the structured visit forms and field notes on paper will also be completed.

STUDY SCHEDULE

Visit	Time	Window	Purpose and Activities
1	Day 0	Baseline	Enroll, consent, baseline data
2	Day 1	before 1m data	Intervention visit 1: health edu
3	Day 3	before 1m data	Intervention visit 2: health edu
4	Day 30	+7 days	1m data collection visit
5	Day 45	before 3m data	Intervention visit 3: self-efficacy
6	Day 60	before 3m data	Intervention visit 4: self-efficacy
7	Day 75	before 3m data	Intervention visit 5: self-efficacy
8	Day 90	±7 days	3m data collection visit
9	Day 105	before 6m data	Intervention check-in 1
10	Day 135	before 6m data	Intervention check-in 2
11	Day 150	before 6m data	Intervention check-in 3
12	Day 165	before 6m data	Intervention check-in 4
13	Day 180	±30 days	6m data collection visit
14	Day 365	±30 days	12m data collection visit
15	Day 366	±7 days	Intervention visit 1: health edu*
16	Day 366	±7 days	Intervention visit 2: health edu*
17	Day 395	±7 days	Intervention visit 3: self-efficacy*
18	Day 410	±7 days	Intervention visit 4: self-efficacy*
19	Day 425	±7 days	Intervention check-in visit 1*
20	Day 440	±7 days	Intervention check-in visit 2*
21	Day 455	±30 days	3m data collection visit*
22	Day 545	±30 days	6m data collection visit*

**Study visits including intervention visits occurring in the control community for participants interested in exercising their option to participate in the intervention.*

6.1 Screening

Based on the lists we obtain of potentially eligible children, caregivers will be contacted by phone, at which point study staff will describe the study, screen for eligibility, and set up a time to enroll and consent if the caregiver is interested. Families will first be contacted about 1 month before enrollment begins.

Screening Visit (Day -30 to -1)

- Confirm eligibility (child ages 1 to 11 years, Yup'ik descent, lives in the study community, has a caregiver age 18 years or older) and interest in participating.
- If screening performed in person, obtain and document consent from potential participant on consent form. Obtain and document assent from children ages 8 to 11 years on assent form.
- If participant is available, collect baseline data (see next section).
- If screening performed by phone, schedule baseline visit, during which time consent and assent will be obtained and baseline data will be collected.
- In case of remote informed consent due to Covid-19 restrictions, send the person a link to a combined consent/assent form in REDCap and conduct informed consent via phone.

6.2 Enrollment/Baseline

Enrollment/Baseline Visit (Visit 1, Day 0)

- Verify inclusion/exclusion criteria.
- Obtain and document consent from participant on study consent form. Obtain and document assent from children ages 8 to 11 years on assent form. If visit conducted remotely, obtain electronic signatures from adult and child.
- Obtain fruit drink survey data, 24-hour food recall and food survey data for each enrolled child, plaque sample from child, hair sample and hair survey from each child participant, and hair sample and hair survey from the primary caregiver in the household (see Appendix for surveys and instructions for self-collection of hair samples).
- If visit conducted remotely, obtain survey data via phone and enter in REDCap and assist participants with collection of hair samples using kit mailed to them. No plaque sample will be collected in case of remote study implementation.
- Provide participants with instructions needed to prepare for Visit 2 (available at home for about 40 minutes, child is present, no anticipated distractions or interruptions).

6.3 Intermediate Visits

Visit 2, Day 1 (before 1m data)

This is the first intervention visit.

- Answer any questions family member has about program.

- Administer the first video health education (about 15 minutes long) (see Manual of Procedures).
- Complete exercises within the video (about 10 minutes long) (see Manual of Procedures).
- Assign first homework assignment (see Manual of Procedures).
- If visit conducted remotely, administer video education and homework via phone or Internet. If visit is in person, use PPE and other precautions consistent with community and UW safety protocols.
- Provide participants with instructions needed to prepare for Visit 3 (available at home for about 30 minutes, have about a gallon of drinking water on hand, child is present, no anticipated distractions or interruptions). In case of remote delivery, send samples of sugar-free water enhancers to the participant by mail.
- Offer exchange of sugar-free drink enhancers for sugared fruit drinks in the home. Family may return the sugared fruit drinks to staff after the visit, arrangements may need to be made to pick them up from the home, or this may need to occur at the next visit.
- CHW completes structured visit form to record participant's compliance with the intervention (e.g., watched the video, children were present, no distractions), intervention components that were delivered, intervention components that were modified or not delivered (along with reasons), follow up items (e.g., get the family a particular flavor sample), and additional notes that will help the CHW deliver subsequent intervention components (see Manual of Procedures).

Visit 3, Day 3 (before 1m data)

This is the second intervention visit.

- Review first homework assignment.
- Administer the second video health education (about 5 minutes long) (see Manual of Procedures).
- Complete exercises within the video including mixing of sugar-free drinks (about 20 minutes long) (see Manual of Procedures). Provide samples of sugar-free water enhancers.
- If visit conducted remotely, administer video education and homework via phone or Internet. If visit is in person, use PPE and other precautions.
- Assign second homework assignment (see Manual of Procedures).
- CHW completes structured visit form (see Manual of Procedures).

Visit 4, Day 30 + 7 days

This is the first data collection visit after the baseline visit (1 month).

- Obtain fruit drink survey data, 24-hour food recall and food survey data for each enrolled child, plaque sample from child, hair sample and hair survey from each child participant, hair sample and hair survey from the primary caregiver in the household, and side effects/adverse events (see Appendix for surveys and instructions for self-collection of hair samples).
- If visit conducted remotely, obtain survey data via phone and enter in REDCap and assist participants with collection of hair samples using kit mailed to them. No plaque sample will be collected in case of remote study implementation.

Visit 5, Day 45 (before 3m data)

This is the third intervention visit.

- Review second homework assignment (see Manual of Procedures).
- Plan for future resistance to behavior change and identify strategies to overcome barriers.
- Assign homework to allow caregivers to document barriers and solutions (see Manual of Procedures).
- Follow up with sugared fruit drink exchange (if applicable and interested).
- Distribute vouchers for sugar-free drinks.
- If visit conducted remotely, administer video education and homework via phone or Internet. If visit is in person, use PPE and other precautions.
- Collect data on side effects/adverse events (see Appendix).CHW completes structured visit form (see Manual of Procedures).

Visit 6, Day 60 (before 3m data)

This is the fourth intervention visit.

- Review homework on barriers and solutions to adoption of sugar-free water enhancers.
- Plan for future resistance to behavior change and identify strategies to overcome barriers.

- If visit conducted remotely, administer homework and plan for overcoming barriers via phone. If visit is in person with Covid-19 risk, use PPE and other precautions.
- Assign homework to track barriers and solutions (see Manual of Procedures).
- Collect data on side effects/adverse events (see Appendix).
- Distribute vouchers for sugar-free drinks.
- Community Health Worker completes structured visit form (see Manual of Procedures).

Visit 7, Day 75 (before 3m data)

This is the fifth intervention visit.

- Review homework on barriers and solutions to adoption of sugar-free water enhancers.
- Plan for future resistance to behavior change and identify strategies to overcome barriers.
- If visit conducted remotely, administer homework and plan for overcoming barriers via phone. If visit is in person, use PPE and other precautions.
- Assign homework for caregivers to continue tracking barriers and solutions.
- Collect data on side effects/adverse events (see Appendix).
- Distribute vouchers for sugar-free drinks.
- CHW completes structured visit form (see Manual of Procedures).

Visit 8, Day 90 ± 7 days

This is the second data collection visit after the baseline visit (3 months).

- Obtain fruit drink survey data, optional 24-hour food recall and food survey data for each enrolled child, plaque sample from children, hair samples and hair survey from each child participant, hair samples and hair surveys from the primary caregiver in the household (or another caregiver if the primary caregiver is not present), and side effects/adverse events for intervention families (see Appendix for surveys and instructions for self-collection of hair samples). Dietary 24 hour food recalls and food survey data may or may not be collected, for all participants, at the discretion of the PI.If visit conducted remotely, obtain survey data via phone and enter in REDCap and assist participants with collection of hair samples using kit mailed to them. No plaque sample will be collected in case of remote study implementation.

Visit 9, Day 105 ± 7 days

This is the first brief check-in visit.

- Check in on families and ask about progress (barriers and solutions), provide encouragement, give vouchers.
- In case of remote implementation, call families on the phone. If in person use PPE and other precautions. Send samples by mail.
- Collect data on side effects/adverse events (see Appendix).

Visit 10, Day 135 ± 7 days

This is the second brief check-in visit.

- Check in on families and ask about progress, provide encouragement, give vouchers.
- In case of remote implementation, call families on the phone. If in person use PPE and other precautions. Send vouchers by mail.
- Collect data on side effects/adverse events (see Appendix).

Visit 11, Day 150 ± 7 days

This is the third brief check-in visit.

- Check in on families and ask about progress, provide encouragement, give vouchers.
- In case of remote implementation, call families on the phone. If in person use PPE and other precautions. Send vouchers by mail.
- Collect data on side effects/adverse events (see Appendix).

Visit 12, Day 165 ± 7 days

This is the fourth brief check-in visit.

- Check in on families and ask about progress, provide encouragement, give vouchers.
- In case of remote implementation, call families on the phone. If in person use PPE and other precautions. Send vouchers by mail.
- Collect data on side effects/adverse events (see Appendix).

Visit 13, Day 180 + 30 days

This is the third data collection visit after the baseline visit (6 months).

- Obtain fruit drink survey data, beverage intake data on the child participants using a validated questionnaire administered to the caregivers, plaque sample from children, hair samples and hair survey from each child participant, hair samples and hair surveys from the primary caregiver in the household (or another caregiver if the primary caregiver is not present), and side effects/adverse events for intervention families (see Appendix for surveys and instructions for self-collection of hair samples). Dietary 24 hour food recalls and food survey data may or may not be collected, for all participants, at the discretion of the PI.
- Conduct semi-structured interviews with caregivers in the intervention arm about their family's consumption of sugared fruit drinks, consumption and availability of sugar-free alternatives, and their experiences throughout the intervention.
- If visit conducted remotely, obtain survey data via phone and enter in REDCap and assist participants with collection of hair samples using kit mailed to them. No plaque sample will be collected in case of remote study implementation.

6.4 Final Study Visit

Visit 14, Day 365 + 30 days

This is the fourth data collection visit after the baseline visit (12 months).

- Obtain fruit drink survey data, beverage intake data on the child participants using a validated questionnaire administered to the caregivers, plaque sample from children, hair samples and hair survey from each child participant, hair samples and hair surveys from the primary caregiver in the household (or another caregiver if the primary caregiver is not present), and side effects/adverse events from families in the intervention arm (see Appendix for surveys and instructions for self-collection of hair samples). Dietary 24 hour food recalls and food survey data may or may not be collected, for all participants, at the discretion of the PI. The fruit drink surveys may be completed by participants using a paper version of the survey form adapted from the versions from the REDCap database.
- If visit conducted remotely, obtain survey data via phone and enter in REDCap and assist participants with collection of hair samples using kit mailed to them. Conduct the post-study interview and provide final instructions by phone. No plaque sample will be collected in case of remote study implementation.

- Conduct semi-structured interviews with caregivers about their family's consumption of sugared fruit drinks, consumption and availability of sugar-free alternatives, and their experiences throughout the intervention; along with post-study feedback on how the program went, any perceived changes in sugared fruit drink behaviors, difficulties and ways to improve the program (see Appendix and Manual of Procedures). Some of the questions from the semi-structured interviews may be answered by participants using a paper based survey, prior to the in-person interview.
- Provide final instructions to participant (e.g., side effects, adverse events, how to contact with questions) (see Manual of Procedures).
- Obtain consent and assent for families and children in the control arm who are interested in participating in the second phase of the study for the modified control community intervention.

6.5 Additional Study Visits for Control Arm

Visit 15, Day 366 ± 7 days

This is the first control community intervention visit.

- The components of this intervention visit will be the same as with Communities A and B (see visit 2 above).
- The control community intervention may be delivered by UW Study staff, or a CHW, in person.

Visit 16, Day 366 ± 7 days

This is the second control community intervention visit.

- The components of this intervention visit will be the same as with Communities A and B (see visit 3 above).
- The control community intervention may be delivered by UW Study staff, or a CHW, in person.

Visit 17, Day 395 ± 7 days

This is the third control community intervention visit.

- The components of this intervention visit will be the same as with Communities A and B (see visit 5 above).

- The control community intervention may be delivered by UW Study staff, or a CHW, in person or by Zoom, phone, or text message.

Visit 18, Day 410 ± 7 days

This is the fourth control community intervention visit.

- The components of this intervention visit will be the same as with Communities A and B (see visit 5 above).
- The control community intervention may be delivered by UW Study staff, or a CHW, in person or by Zoom, phone, or text message.

Visit 19, Day 425 ± 7 days

This is the first brief check-in visit.

- Check in on families and ask about progress (barriers and solutions), provide encouragement.
- In case of remote implementation by UW study staff, families will be called on the phone. If a CHW is available, the check-in visit may be completed in person or by Zoom, phone, or text message.

Visit 20, Day 440 ± 7 days

This is the second brief check-in visit.

- Check in on families and ask about progress (barriers and solutions), provide encouragement.
- In case of remote implementation by UW study staff, families will be called on the phone. If a CHW is available, the check-in visit may be completed in person or by Zoom, phone, or text message.

Visit 21, Day 455 +/- 30 days

This is the first data collection visit after the 12-month data collection from the main study (3m data collection visit for controls).

- Obtain fruit drink survey data, beverage intake data on the child participants using a validated questionnaire administered to the caregivers, plaque sample

from children, hair samples and hair survey from each child participant, hair samples and hair surveys from the primary caregiver in the household (or another caregiver if the primary caregiver is not present), and side effects/adverse events from families in the intervention arm (see Appendix for surveys and instructions for self-collection of hair samples). Dietary 24 hour food recalls and food survey data may or may not be collected, for all participants, at the discretion of the PI.

- Conduct semi-structured interviews with caregivers about their family's consumption of sugared fruit drinks, consumption and availability of sugar-free alternatives, and their experiences throughout the intervention; along with post-study feedback on how the program went, any perceived changes in sugared fruit drink behaviors, difficulties and ways to improve the program (see Appendix and Manual of Procedures).

Visit 22, Day 545 +/- 30 days

This is the second data collection visit after the 12-month data collection from the main study (6m data collection visit for controls).

- Obtain fruit drink survey data, beverage intake data on the child participants using a validated questionnaire administered to the caregivers, plaque sample from children, hair samples and hair survey from each child participant, hair samples and hair surveys from the primary caregiver in the household (or another caregiver if the primary caregiver is not present), and side effects/adverse events from families in the intervention arm (see Appendix for surveys and instructions for self-collection of hair samples). Dietary 24 hour food recalls and food survey data may or may not be collected, for all participants, at the discretion of the PI.
- Conduct semi-structured interviews with caregivers about their family's consumption of sugared fruit drinks, consumption and availability of sugar-free alternatives, and their experiences throughout the intervention; along with post-study feedback on how the program went, any perceived changes in sugared fruit drink behaviors, difficulties and ways to improve the program (see Appendix and Manual of Procedures).
- Provide final instructions to participant (e.g., side effects, adverse events, how to contact with questions) (see Manual of Procedures).

STUDY PROCEDURES/EVALUATIONS

7.1 Study Procedures/Evaluations

Study staff and CHWs will work with store staff in the 2 intervention communities to make sure the sugar-free water enhancers are available throughout the study period. This will involve the CHW visiting the stores weekly to monitor availability, to work with stores to order more if needed, to check with families to make sure they are not experiencing any difficulties finding or buying the drinks, and to problem solve with store owners to address any unanticipated barriers to families finding or buying the drinks. For all in-person study procedures, including store visits, the CHWs will use PPE and other precautions. UW study staff will also work with the store in the control community to make sure the sugar-free water enhancers are available throughout the control community intervention.

Data Collection Frequency. In all study communities, there will be 5 data collection visits (baseline, 1 month, 3 months, 6 months, and 12 months) which will take place separately from the intervention visits. In the control community, there will be 2 additional data collection visits (3-months and 6-months) after the initial 12-month study period.

Data Collection Tools. At the baseline data collection visit, demographic data, fruit drink survey data, 24-hour food recall and food question data will be collected for each participating child, a hair sample from the child(ren) and caregiver. All survey data will be collected electronically via laptop using a secure REDCap database, with survey data collection via phone in the case of remote implementation. The **demographic survey** will include standard questions found in national surveys that are validated (e.g., date of birth, race, household income, etc.). The **fruit drink survey** was developed by the study team and tested in the field with Yup'ik caregivers (see Manual of Procedures). The purpose of the fruit drink survey is to assess changes in knowledge, beliefs, and self-efficacy related to oral health, sugar-free drinks, and ability to help their children switch from sugared to sugar-free drinks. These measures will be part of the mediation analyses to assess for mechanisms underlying the intervention. For the 12-month data collection visit (and control community intervention data collection visits) the fruit drink survey may be completed by participants using a paper version of the survey form adapted from the versions on the REDCap database.

The **24-hour food recall**, a validated method, will be used to measure sugared fruit drink intake at baseline and 1-month. There will also be a **food survey** to measure food insecurity, breastfeeding, and other relevant questions related to food intake. Additional 24-hour food recall interviews and food surveys may or may not be conducted at 3-months, 6-months, and 12-months.

The **Beverage Questionnaire**, a validated beverage intake assessment tool (BEVQ-15) will be administered to caregivers to measure intake of several beverages for each of their enrolled children including: sugared fruit drinks, sweetened juice, 100% juice,

sugar-free Kool-Aid, soda pop/soft drinks, diet soda pop/articficially sweetened soft drinks (not including sugar-free Kool-Aid), sports drinks/energy drinks and milk. The

The **plaque sample** will be collected and banked at the UW for future analyses to determine the effects of the intervention on bacteria in the mouth. The **hair sample** will be used to measure added sugar intake using a validated biomarker (Nash et al. 2013). The hair sample is accompanied by a short **hair survey** regarding hair condition (e.g., bleached, dyed, etc.). The plaque sample will not be collected in case of remote study implementation.

A **side effects and adverse events form** will be used to record data on potential and other events that could come from excess intake of the sugar-free water enhancers, as a measure of safety, and to allow our team to intervene as needed to minimize any potential side effects associated with the intervention. This form will only be collected from intervention families.

At subsequent data collection visits, the same information will be collected except for demographic data, 24-hour food recalls, and food surveys. The 6-month and final visit (12-month) will include **semi-structured interviews** with caregivers to qualitatively assess perceived changes in sugared fruit drink consumption, behavior changes, obtain feedback about the program, benefits and drawbacks, and ways to improve the program. Incentives will be given at each data collection visit. For the 12-month data collection visit (and control community intervention data collection visits), some of the questions from the semi-structured interviews may be answered by participants using a paper-based survey, prior to the in-person interview.

7.2 Laboratory Procedures/Evaluations

7.2.1 Clinical Laboratory Evaluations

Each collected hair sample will consist of about 20 strands of hair and will be stored in a clear plastic Ziploc bag labeled with the participant's study ID. Each hair sample will be tied together with a binder clip to indicate the section closest to the scalp that will undergo isotope analyses. Shorter hair samples that cannot be tied will be collected on in small piece of foil. One centimeter of hair corresponds to approximately 1 month of growth and reflects added sugar intake from the previous 1 to 2 months. Hair samples will be hand carried to UW after each data collection visit and samples will be batch mailed from Seattle to UAF for processing and analysis. In the case of remote study implementation due to Covid-19 all hair sampling kits will be mailed to participants before study start, labeled with their ID numbers. Each family will be provided with detailed paper instructions regarding how to obtain the sample prior to a video or phone call with UW study staff at baseline (see Appendix M). During the call with UW study staff the staff person will walk the participant through the sampling procedures while they are on the phone and explain how to mail the samples to UW. If CHWs are able to visit participants in the home using PPE and other precautions, the CHW can also support participants' collection of hair. Caregivers will collect their own hair and the hair

from their children who are enrolled in the study. Caregivers will mail hair samples to UW using a pre-addressed stamped envelope. The 1cm section of the hair sample most proximal to the scalp will be cleaned, prepared, and analyzed for carbon and nitrogen isotope ratios using continuous flow isotope ratio mass spectrometry at the Alaska Stable Isotope Facility (Nash et al. 2014). Trained staff are employed by the facility. Hair samples will be solvent cleaned with sonication to remove hair care products and residues, and carbon and nitrogen isotope ratios will be analyzed using continuous flow isotope ratio mass spectrometry. Added sugar intake will be generated from carbon and nitrogen isotope ratios using previously estimated coefficients for the Yup'ik population (Nash et al. 2013).

7.2.2 Specimen Preparation, Handling, and Storage

All plaque samples will be hand carried to UW from the study sites, processed and stored according to specimen collection kit manufacturer instructions, locked within the UW School of Dentistry. They will be stored until funding is obtained for future microbiological analyses. All hair samples will be stored at room temperature in the PI's private office at UW until they are ready to be sent to UAF for processing. The plaque samples will be destroyed by end of 2027, or approximately 5 years after the study start.

7.2.3 Specimen Shipment

Hair samples received from participants will be sent from UW to UAF via FedEx after each data collection visit (5 separate FedEx mailings).

ASSESSMENT OF SAFETY

8.1 Specification of Safety Parameters

Safety concerns include potential side effects associated with excess intake of the artificial sweeteners in the sugar-free water enhancers (sucralose and ace-K). Side effects include gastrointestinal effects, stomachache, and diarrhea. Additional side effects may include allergic reactions, changes in insulin sensitivity, alterations in gastrointestinal microbiota, weight gain, and decreased satiety. Precautions will be taken as part of the intervention to educate caregivers on how to minimize intake of the target sugar-free water enhancers. All local health aides will be educated about the intervention and the potential for side effects in the case of excess intake and management protocols.

Random samples of sugar-free water enhancers (Tang, Kool-Aid Grape, Kool-Aid Tropical Punch, Kool-Aid Cherry) were obtained to evaluate the concentrations of the 2 artificial sweeteners (sucralose and ace-K). When mixed according to instructions, each 8oz serving contains an average of 43mg of sucralose and 15 mg of ace-K (Tang contains no ace-K). Testing among study staff was conducted to identify the possibility of diluting the drinks with water to increase the maximum volume that could be consumed by study participants. Tables were created that the CHW will use with caregivers to show the maximum amount of sugar-free fruit drink children can consume each day (see Manual of Procedures). Pilot families in the YK Delta tried the diluted recipes and these were well accepted by children and caregivers.

At each study visit, a CHW or study staff will ask the caregiver about any side effects experienced from the sugar-free water enhancers and will work with the caregiver to assess severity, source, and remedies. If the symptoms or side effects have persisted for more than 48 hours, the CHW will contact the Research Coordinator and Study PI to report the problem to a local health aide. The medical health aides are individuals who live in the communities and are the front-line primary medical care providers in the study communities. They will be asked to follow up with the family and determine the best course of treatment (e.g., monitor, hydration therapy, other). Between study visits, if a caregiver suspects that their child is experiencing side effects associated with the sugar-free water enhancers, they will be asked to contact the CHW. The CHW will then contact the Research Coordinator and Study PI. The Study PI will work with the caregiver and medical health aide to identify the possible cause of the side effects or the relationship of the adverse events to the study intervention.

Side effects/adverse events will be classified as mild, moderate, or severe (see Manual of Procedures). If the side effects are mild or moderate, the child's sugar-free water enhancer intake will be reduced, and the child's side effects will be monitored over the next 48 hours to see if the symptoms resolve. If symptoms are severe or continue past 48 hours, the caregiver will be asked to stop giving the child the sugar-free drinks and to visit the local health aide. If the child's symptoms resolve, caregivers can elect to continue giving their child the sugar-free drinks under close supervision. If the same

symptoms or side effects return a second time, the child's participation in the intervention will be terminated. The child and caregiver will be encouraged to still be involved in all subsequent data collection visits.

All side effects will be recorded in the study database by the Research Coordinator. The following data will be recorded: participant ID, date of onset of symptoms, severity of symptoms, length of symptoms, any health care services sought, advice given by health care provider, and caregiver decision on whether to continue participating with the intervention. Expected adverse events will be reported to the UW IRB during annual continuing review. Information will be provided on how the adverse event was managed and resolved. The YKHC's Chair of the HSC will be notified immediately of any adverse event. We will also report all unexpected adverse events and serious adverse events to UW IRB within 10 business days. All serious adverse events and unanticipated problems will be reported to NIDCR within 10 business days. In the case of remote implementation of the study, side effects and adverse events will be assessed by the CHW during online study visits or via the phone (and entered into REDCap) and by UW study staff during data collection via phone.

8.2 Unanticipated Problems

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to subjects or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.3 Adverse Events

An adverse event is any untoward or unfavorable medical occurrence in a human participant, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with participation in the research, whether or not considered related to participation in the research.

8.4 Serious Adverse Events

A serious adverse event (SAE) is one that meets one or more of the following criteria:

- Results in death
- Is life-threatening (places the subject at immediate risk of death from the event as it occurred)
- Results in inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant disability or incapacity
- Results in a congenital anomaly or birth defect
- An important medical event that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

8.5 Time Period and Frequency for Event Assessment and Follow-Up

The PI will record all events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the Community Health Worker or Study Staff will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

8.6 Characteristics of an Adverse Event

Each event will be recorded on an appropriate case report form that includes assessment of the characteristics defined below. These characteristics, along with the frequency of an event's occurrence, will be considered in determining if the event is an unanticipated problem.

8.6.1 Relationship to Study Intervention

To assess relationship of an event to study intervention the following guidelines are used:

1. Related (Possible, Probable, Definite)
    a. The event is known to occur with the study intervention, and/or
    b. There is a temporal relationship between the intervention and event onset and/or
    c. The event abates when the intervention is discontinued, and/or

d. The event reappears upon a re-challenge with the intervention.

2. Not Related (Unlikely, Not Related)

    a. There is no temporal relationship between the intervention and event onset, and/or

    b. An alternate etiology has been established.

8.6.2 Expectedness

The Study PI will determine whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the intervention.

8.6.3 Severity of Event

The following scale will be used to grade adverse events:

1. Mild: no intervention required; no impact on activities of daily living (ADL)

2. Moderate: minimal, local, or non-invasive intervention indicated; moderate impact on ADL

3. Severe: significant symptoms requiring invasive intervention; subject seeks medical attention, needs major assistance with ADL

8.7 Reporting Procedures

8.7.1 Unanticipated Problem Reporting

Incidents or events that meet the OHRP criteria for unanticipated problems require the creation and completion of an unanticipated problem report form. OHRP recommends that investigators include the following information when reporting an adverse event, or any other incident, experience, or outcome as an unanticipated problem to the IRB/HSC:

- appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
- a detailed description of the adverse event, incident, experience, or outcome;
- an explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem;
- a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

To satisfy the requirement for prompt reporting, unanticipated problems will be reported using the following timeline:

- Unanticipated problems will be reported to the UW IRB within 10 business days of the investigator becoming aware of the event. The investigator will submit a Reportable New Information form in the UW electronic IRB submission system. Reporting will occur immediately to YKHC's HSC Chair.
- All unanticipated problems will be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and OHRP within one month of the IRB's receipt of the report of the problem from the investigator.

All unanticipated problems will be reported to NIDCR concurrently with reporting to the IRB. Serious Adverse Event Reporting

Any AE meeting the specified Serious Adverse Event criteria will be submitted on an SAE form to NIDCR's centralized safety system via Rho Product Safety. This report may be sent by fax or email. Once submitted, Rho Product Safety will send a confirmation email to the investigator within 1 business day. The investigator should contact Rho Product Safety if this confirmation is not received. This process applies to both initial and follow-up SAE reports.

SAE Reporting Contact Information:

- Product Safety Fax Line (US): 1-888-746-3293
- Product Safety Fax Line (International): 919-287-3998
- Product Safety Email: rho_productsafety@rhoworld.com

General questions about SAE reporting can be directed to the Rho Product Safety Help Line (available 8:00AM – 5:00PM Eastern Time):

- US: 1-888-746-7231
- International: 919-595-6486

The study's clinically responsible individual will complete a Serious Adverse Event Form and submit via email within the following timelines:

- All deaths and immediately life-threatening events, whether related or unrelated, will be recorded on the Serious Adverse Event Form and submitted to Rho Product Safety within 24 hours of site awareness.
- Serious adverse events other than death and immediately life-threatening events, regardless of relationship, will be reported by email or fax within 10 days of site awareness.

All SAEs will be followed until resolution or stabilization.

In addition to being reported to NIDCR, all serious adverse events will be reported to the University of Washington Human Subject Division and IRB within 10 business days of the investigator becoming aware of the event. The investigator will submit a Reportable New Information form in the electronic IRB submission system at the University of Washington. The YKHC HSC will be notified immediately.

8.7.2 Reporting of Safety Events to FDA

The artificial sweeteners (sucralose and acesulfame potassium) in the sugar-free water enhancers are considered food additives by the US FDA. If there are any adverse events observed during or after the study, the study staff will report them to the FDA by phone at 240-402-2405, which is the FDA Center for Food Safety and Applied Nutrition reporting hotline phone number. There is also the option to submit a Medwatch form at *https://www.fda.gov/safety/report-problem-fda/how-report-non-emergency#food.* We will report adverse events using whichever methods is available to the PI at the time of reporting.

8.7.3 Reporting of Pregnancy

There are no specific pregnancy-related policies and procedures.

8.8 Halting Rules

If there is a significant number of children who experience symptoms or side effects that are thought to be associated with the sugar-free water enhancers (more than 20%), an ad hoc safety review will be convened. The objective of the safety review is to decide whether the study (or intervention for an individual or study cohort) should continue per protocol, proceed with caution, be further investigated, be discontinued, or be modified and then proceed. Suspension of enrollment (for a particular group, a particular study site, or for the entire study) is a potential outcome of a safety review.

STUDY OVERSIGHT

In addition to the PI's responsibility for oversight, study oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) appointed by the NIDCR. The DSMB will operate under the rules of an NIDCR-approved charter that will be approved at the organizational meeting of the DSMB. The conduct of the DSMB and rules regarding how often the Board will meet will be defined by the DSMB charter for the study. At this time, most data elements that the DSMB needs to assess will be clearly defined. It is anticipated that the DSMB will meet at least once per year via teleconference to assess safety and efficacy data, study progress, and data integrity for the study. If safety concerns arise, more frequent meetings may be held. The DSMB will operate under the rules of an NIDCR-approved charter that will be approved at the organizational meeting of the DSMB. At this time, most data elements that the DSMB needs to assess will be clearly defined. The DSMB will provide recommendations to the NIDCR.

CLINICAL SITE MONITORING

Clinical site monitoring is conducted to ensure that the rights of human subjects are protected, that the study is implemented in accordance with the protocol and/or other operating procedures, and that the quality and integrity of study data and data collection methods are maintained. Monitoring for this study will be performed by the NIDCR's Clinical Research Operations and Management Support (CROMS) contractor. The monitor will evaluate study processes and documentation based on the International Council for Harmonisation (ICH), E6: Good Clinical Practice guidelines (GCP).

Details of clinical site monitoring will be documented in a Clinical Monitoring Plan (CMP). The CMP will specify the frequency of monitoring, monitoring procedures, the level of clinical site monitoring activities (e.g., the percentage of participant data to be reviewed), and the distribution of monitoring reports. Some monitoring activities may be performed remotely, while others will take place at the study site(s). Staff from CROMS will conduct monitoring activities and provide reports of the findings and associated action items in accordance with the details described in the CMP. Documentation of monitoring activities and findings will be provided to the site study team, the study PIs, NIDCR-OCTOM, and NIDCR Program staff. The NIDCR reserves the right to conduct independent clinical site monitoring as necessary.

STATISTICAL CONSIDERATIONS

11.1 Study Hypotheses

11.1.1 Primary Hypotheses

1. Children in the intervention arm will have lower added sugar intake from baseline to 6 months compared to children in the no-treatment control arm (measured though hair biomarker).

   Null hypothesis: The average change (reduction) in added sugar intake between baseline and 6 months will be the same for children in the intervention arm and no-treatment control arm.

   Alternative hypothesis: The average change (reduction) in added sugar intake between baseline and 6 months will be different for children in the intervention arm and no-treatment control arm.

11.1.2 Secondary Hypotheses

1. Caregivers in the intervention arm will have lower added sugar intake from baseline to 6 months compared to caregivers in the no-treatment control arm (measured though hair biomarker).

2. Children in the intervention arm will have sustained lower added sugar intake 6 months after the end of the intervention as compared to children in the no-treatment control arm.

11.1.3 Exploratory Hypotheses

1. Caregivers in the intervention arm will have greater improvement in knowledge, beliefs, and self-efficacy related to oral health, sugar-free drinks, and ability to help their children switch from sugared to sugar-free drinks at the end of the intervention as compared to caregivers in the non-treatment control arm.

2. Children in the intervention arm will have an altered oral microbiome, due to changes in sugared fruit drink and added sugar intake, as measured by mutans

streptococci levels and oral microbiome features through analysis of oral plaque samples.

3. Children in the intervention arm will have lower sugared fruit drink intake after receiving the intervention compared to children in the no-treatment control arm.

   Null hypothesis: The average sugared fruit drink intake in ounces at 6 months and 12 months will be the same for children in the intervention arm and no-treatment control arm.

   Alternative hypothesis: The average sugared fruit drink intake in ounces at 6 months and 12 months will be different for children in the intervention arm and no-treatment control arm.

SAMPLE SIZE CONSIDERATIONS

There are about 127, 175, and 108 children ages 1 to 11 years in communities A, B, and C respectively. Some are siblings or relatives living in the same home. Based on a survey of 123 households in the 3 study communities, for the power calculations, each household was assumed to have an average of 2.15±1.23 children per household. In addition, to account for the clustering of children within households, a conservative intra-family correlation (IFC) of 0.3 was assumed, but an IFC as high as 0.5 was assumed to assess the effect on power (Eldridge et al. 2006).

Participation in previous studies has been over 60%. Based on our pilot study, it is feasible and reasonable to enroll at least 50% of eligible children. Communities A and B will be in the intervention arm (expected N=136) and community C will be in the control arm (expected N=56). For the power determination, a 15% to 25% attrition rate was estimated by 6 months, but it is expected that actual attrition will be less than 10% by the 6-month follow-up.

Power is determined for comparing the average reduction from baseline to 6 months between children in the intervention arm and no-treatment control arm for the primary outcome: added sugar intake per day (determined by hair samples). Based on pilot data from 54 Yup'ik children ages 6 to 17 years, the mean±SD baseline added sugar intake, as measured by hair samples, is expected to be 193.0±43.6 grams per day. (Chi et al. 2015). A correlation of 0.6 is assumed between the measures at baseline and 6 months to determine the standard deviation for reduction from baseline to 6 months.

The power is calculated using a 2-sided significance level of alpha=0.025 to control the type I error for the testing of the primary outcome, and using a 2-sample t-test to compare the average reduction between the intervention arm and no-treatment control arm using the expected (unequal) sample sizes and adjusted for the IFC and attrition (Eldridge et al. 2006).

In the intervention arm, added sugar intake is expected to drop by 20% to 40%. Minimal changes are expected in the control arm, but for the power calculations have assumed modest reductions in the control arm. These estimates are based on a previous beverage substitution RCT that showed 88% reduction in the intervention group for the number of sugared beverages consumed per day and 3 school-based studies showing 20% to 26% reductions in the intervention groups (Ebbeling et al. 2012; James et al. 2004; Sichieri et al. 2014; Singh et al. 2009).

The power to demonstrate a difference between the intervention arm and control arm for the reduction from baseline to 6 months of added sugar intake is reported in the Table below. Power is high (>85%) for the majority of scenarios. For example, power is 98% to demonstrate an intervention effect for added sugar intake assuming a 30% reduction in the intervention arm and a 5% reduction in the control arm.

Table. Power to demonstrate a difference between the intervention and control groups for a reduction from baseline to 6 months in added sugar intake at a 2-sided alpha = 0.025 significance level.

Added sugar intake			
% Reduction		Power	
Intervention	Control	IFC=0.3	(IFC=0.5)
40%	5%	99%	(99%)
30%	**5%**	**98%**	(95%)
20%	1%	86%	(76%)
40%	10%	99%	(99%)
30%	10%	89%	(81%)
20%	2%	81%	(71%)

The expected numbers of children in the intervention arm and control arm will provide adequate power to test secondary hypotheses about a sustained reduction in sugared fruit drink intake and added sugar intake 6 months after the end of the intervention for children in the intervention arm. Based on a 2-sided 0.05 significance level, the power is >80% to detect a difference of 0.60 standard deviation units in the change from baseline to 12 months between the two arms. For example, power is 88% to demonstrate an intervention effect for a 20% reduction in the intervention arm versus a 2% reduction in the control arm for added sugar intake. The expected number of caregivers in the intervention arm is N=51 and in the control arm is N=21, and these sample sizes also provide adequate power to the test secondary hypothesis about a greater reduction in added sugar intake at the end of the intervention for caregivers in the intervention arm as compared to the control arm. Based on a 2-sided 0.05 significance level, the power is >80% to detect a difference of 0.75 standard deviation units in the change from baseline to 6 months between the 2 arms. For example, power is 81% to demonstrate an intervention effect for a 25% reduction in the intervention arm versus a 5% reduction in the control for the caregiver's added sugar intake.

PLANNED INTERIM ANALYSES (IF APPLICABLE)

No interim analysis is planned for stopping the study early

13.1 Final Analysis Plan

The analysis will be based on the intent to treat principle. Demographic variables will be summarized for the intervention arm and no-treatment arm at baseline and at each follow-up for all outcome measures and behavioral survey variables, as well as baseline demographics. Quantitative measures will be summarized by the mean and standard (or median and interquartile range for measures with a skewed distribution) and categorical measures will be summarized by frequency and percentage.

Linear regression analyses will be used to test if the average change in added sugar intake between baseline and 6 months is the same for children in the intervention arm and no-treatment control arm. A 2-sided 0.025 significance level will be used for the tests of the primary outcome. Generalized estimating equation (GEE) methodology will be used to fit the linear regression models using robust standard errors that account for potential clustering of outcomes within a household and allow for heteroscedasticity (Hardin and Hilbe 2003). Additional linear regression analyses will compare the 2 arms adjusted for baseline characteristics to assess for potential confounding and to assess for moderation of the intervention effect on child sugar intake by baseline characteristics, including child age, child sex, and traditional diet. In addition, to assess the effects of sex as a biological variable, separate estimates for the intervention effect on added sugar intake will be reported by child sex.

Similar linear regression analyses will be performed for the secondary outcomes for changes in caregivers' added sugar intake, knowledge, beliefs and self-efficacy. Outcomes at 1 month and 3 months will be summarized to elucidate the changes from baseline to 6 months in the intervention arm and no-treatment arm. Linear regression analyses will also be used to test the exploratory hypothesis that children in the intervention arm will have decreased sugared fruit drink intake after having received the intervention (at 6 months and 12 months).

A secondary hypothesis is that greater improvements in caregiver knowledge, beliefs, and self-efficacy in the intervention arm as compared to the no-treatment control will result in sustained reductions in sugar fruit drink intake and added sugar intake for children in the intervention arm 6 months after the intervention ends. This will support the hypothesis that behaviors are the mechanisms by which sugared fruit drink intake and added sugar intake are reduced. To assess this hypothesis, we will used linear regression analysis to test if the average chang inadded sugar intake between baseline and 12 months is the same for children in the intervention arm and no-treatment control arm. Mediation analysis will then be used to assess if changes between baseline and 6 months in caregiver's knowledge, beliefs, and self-efficacy mediate the change between baseline and 12 months in children's sugar intake. The initial mediation analyses will follow the traditional approach of Baron and Kenny (1986) but the formal test for mediation will be based on a product of coefficients approach that directly tests for a

non-zero indirect effect using a bias-corrected bootstrap confidence interval (Hayes 2013). The test for mediation will be done for each mediator individually and for all mediators as a group.

Missing data will be managed as described in Strategies for Recruitment and Retention. Information will be collected on the reasons for discontinuation and withdrawal from the study. This information will be used to assess whether there is non-ignorable nonresponse. In the case of non-ignorable nonresponse, the method of Rotnizky et al. (1998) based on augmented inverse probability of censoring weighted estimating equations, will be used to perform a sensitivity analysis to examine how the estimated intervention effect on the primary outcome measures changes over a range of plausible values for the nonresponse mechanism. Otherwise, multiple imputation methods will be used to account missing outcomes and to derive intervention effect estimates consistent with the intent to treat principle (Schafer 2005). The goal of the study is to retain >75% of those enrolled. Statistical analysis will be performed using SAS Version 9.4 (SAS Institute Inc., Cary, North Carolina) and R version 3.5 (**R** Foundation for Statistical Computing, Vienna, Austria).

To assess the hypothesis that children in the intervention arm will have an altered oral microbiome, due to changes in sugared fruit drink and added sugar intake, data from a microbiome analysis of oral plaque samples collected at five data collection timepoints (baseline, 1 month, 3 month, 6 month and 12 month) will be used to compare changes in mutans streptococci levels and other oral microbiome features (e.g., species abundance, composition and diversity). Linear and log-lnear regression will be used to test separately if there are changes in mutans streptocci levels and other oral microbiome features and to compare changes in children in the intervention versus control communities. Robust standard errors will be used with linear regression and log-linear regression to account for potential heteroscedasticity and overdispersion.

Similar analyses will be conducted on the 3m and 6m data collected from families in the control community who receive the modified intervention.

SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

Source data include electronically captured survey data (demographic survey data, fruit drink survey data, food recall data, beverage questionnaire data, hair survey data, side effects and adverse events data); 24-hour recall data collected electronically; post-intervention exit interview data that will be recorded, transcribed, and coded; and paper field notes generated by staff and CHWs on the structured visit form. In the case of remote implementation, the structured visit form and side effects and adverse events form will be electronically captured using REDCap.

Study staff will maintain appropriate research records for this study, in compliance with ICH E6, Section 4.9 and regulatory and institutional requirements for the protection of confidentiality of participants. All data will be stored in the Study PI's locked private office within locked filing cabinets and on password-protected servers within the UW School of Dentistry. REDCap data will be stored on the UW REDCap server. Only study staff will have access to the data on a need-to-access basis. Data will be transmitted via secure FTP. Study staff will permit authorized representatives of NIDCR and regulatory agencies to examine (and when required by applicable law, to copy) research records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress, and data validity.

QUALITY CONTROL AND QUALITY ASSURANCE

The PI will ensure that all elements of the proposed work are performed, and the data are generated, recorded, and reported in compliance with Good Clinical Practice (GCP) and other applicable regulatory requirements. This will be done through training prior to the start of study; establishing shared mental models and goals; rigorous periodic review of study progress and processes; and vigilant data safety and monitoring processes.

The PI will ensure quality measures are in place for all aspects of this study from training of staff and recruitment of participants to implementation of the protocol and data management. All aspects of the consenting process, including the informed consent form and associated documentation to confirm adherence to the consent process, are further discussed in the Manual of Procedures.

UW study staff working with the PI will ensure that quality control and assurance protocols are operationalized in the field as planned. The team will work together to correct procedures that are not in compliance with the protocol.

Quality control and assurance measures are divided into 3 categories: 1) trainings and fidelity monitoring to ensure proper delivery of the intervention; 2) monitoring for study recruitment; and 3) staff trainings and checklists to ensure accurate and complete data collection.

Trainings and fidelity monitoring. Multiple trainings will be held to prepare CHWs to serve as study interventionists. The trainings will introduce them to the intervention and how each intervention piece is delivered. All trainings will be logged and the log will be maintained as part of the trial essential documents. The training components and procedures are described in detail (see Manual of Procedures). Exams will be used to test them on key concepts and passing grades will be necessary before a CHW can move onto the next stage of training. Trainees will be given opportunities to practice delivering the intervention with each other and with study staff using materials that will be used for the actual intervention (e.g., video with health educational materials loaded onto iPads, games, sugar demonstration props). Fidelity checklists will be used to assess the quality of practice intervention delivered by the CHW or UW study staff (for the control group intervention). There will be multiple levels of certification to ensure that CHWs or UW study staff can deliver the intervention with increasing sophistication. Once an interventionist is fully certified, they will be monitored as they deliver the intervention to families. The fidelity checklist will be used to assess intervention delivery and corrections will be made as needed via in-person feedback and re-trainings. During each visit, the interventionist will ensure that the participant continues to meet all eligibility requirements. In case of remote implementation of the study CHWs will be assessed via participation in video sessions to observe the quality of the intervention delivery. Retraining of the CHWs will be done as needed based on the quality of the sessions observed by the fidelity monitor. For the delivery of the control community intervention, UW study staff will be trained by a co-investigator to ensure achievement

of advanced and final certification in order to deliver the intervention components, in lieu of a CHW if they are not available. Fidelity monitoring benchmarks and requirements for ongoing monitoring (i.e., field notes) will be consistent for UW study staff and CHWs.

Monitoring for study recruitment. Monthly reports will be generated to monitor enrollment. These monitoring reports will be discussed at team meetings to ensure adequate progress on the study goals. Advanced problem solving and solution generation exercises during these meetings will help prevent the group from falling behind on goals.

Staff trainings and checklists. Staff trainings will be held to ensure accurate and complete data collection and storage (e.g., 24-hour dietary recall, hair samples, plaque collection). Backup plans will ensure high-quality data collection in cases where unanticipated problems arise. Participant-level checklists will be used to ensure that all necessary data elements are collected at each data collection visits. All data documents will be reviewed for completeness within 24 hours so that relevant corrections or unintentionally missing data can be identified and possibly collected, and to identify necessary AE/SAE reporting. Data accuracy will be confirmed at level of data entry by the Lead Study Coordinator. Staff training methods will include hands on training, practice sessions, validation exercises to ensure accuracy, and certification.

ETHICS/PROTECTION OF HUMAN SUBJECTS

16.0 Ethical Standard

The investigator will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, as drafted by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46 and/or the ICH E6.

16.1 Institutional Review Board

The protocol, informed consent form, assent form, recruitment materials, and all participant materials will be submitted to the UW IRB for review and approval. Approval of these materials must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented in the study.

16.2 Informed Consent Process

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. Extensive discussion of risks and possible benefits of study participation will be provided to participants and their families. The consent form describing in detail the study procedures and risks will be given to the participant (see Manual of Operations). Consent forms will be IRB-approved, and the participant is required to read and review the document or have the document read to him or her. A Research Coordinator will explain the research study to the participant and answer any questions. The participant will sign the electronic informed consent document prior to any study-related assessments or procedures. Participants will be given the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. They may withdraw consent at any time throughout the course of the study. An electronic copy of the signed informed consent document will be emailed or printed on site to give to participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline to participate in this study. In the case of remote implementation of the study, the REDCap electronic consent form will be emailed to the adult participant using a personalized REDCap link. A trained UW staff member will then discuss the form with the adult on the phone and, if the caregiver agrees, he/she will sign the form electronically. In case of Internet connectivity problems a paper consent form will be mailed to the adult and consent will be explained by phone with the signed paper consent form returned to the UW in a pre-addressed envelope.

16.3 Exclusion of Women, Minorities, and Children (Special Populations)

The study will exclude children younger than age 1 year and older than age 11 years at baseline from the study. The reason is that the intervention focuses on reducing Tang

and Kool-Aid intake which is more common among younger children compared to older children. We exclude children younger than age 1 year to eliminate any potential safety concerns associated with sugar-free water enhancer intake. The study also focuses on Alaska Native children and therefore will exclude non-Alaska Native children.

16.4 Participant Confidentiality

Participant confidentiality is strictly held in trust by the investigators, study staff, and the study sponsor and their agents. This confidentiality is extended to cover testing of biological samples in addition to any study information relating to participants.

The study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the study sponsor.

The study monitor or other authorized representatives of NIDCR may inspect all study documents and records required to be maintained by the investigator for the study participants.

16.4.1 Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical, or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (https://humansubjects.nih.gov/coc/index). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

16.4.2 NIH Data Sharing Policies

As described in section 17, it is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see https://grants.nih.gov/policy/sharing.htm). PIs and funding recipient institutions will ensure that all mechanisms used to share data include proper plans and safeguards to protect the rights and privacy of individuals who participate in NIH-sponsored research.

16.5 Future Use of Stored Specimens and Other Identifiable Data

As part of the consent process, additional permission will be obtained to conduct analyses of the banked plaque sample, but only to answer specific questions related to how the intervention worked and for whom the intervention was responsive through mutans streptococci enumeration and the oral microbiome composition. We will not use the biospecimens for any commercial purpose. We will make no attempt to identify participants or contact participants to which the plaque specimens pertain. We will make no disclosure of the plaque biospecimen to third parties without written consent of YKHC. We will make no secondary research uses of the plaque biospecimens other than the uses identified in the protocol. Plaque biospecimens will not be used in clinical trials or for diagnostic purposes involving humans. Plaque biospecimens are to be used only in the UW's research facilities or with collaborators working under the direct supervision of the study PI. The plaque samples will be destroyed by end of 2027, approximately 5 years after study start. Policies and procedures for community, ethical, and scientific review and approval will always apply. This policy is a core part of both the strong community-researcher consensus and agreement, and also of the team's respect for the Alaska Native people, communities, and entire regions. In case of remote implementation of the study, plaque sampling will not occur.

DATA HANDLING AND RECORD KEEPING

The investigators are responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents will be completed in a neat, legible manner to ensure accurate interpretation of data. The investigators will maintain adequate case histories of study participants and source documentation.

17.0 Data Management Responsibilities

Data collection and accurate documentation are the responsibility of the study staff under the supervision of the investigator. All source documents and laboratory reports will be reviewed by the study team, who will ensure that they are accurate and complete. Side effects and adverse events will be reviewed by the PI.

17.1 Data Capture Methods

There are multiple data capture methods: paper, electronic, biological, and digitally recorded. All paper data will be entered into the study REDCap database.

Paper field notes, if applicable, will be hand carried from field research sites to the UW, at which point they will be scanned and saved onto secure, password-protected servers. The original notes will be stored in locked filing cabinets in the Study PI's secure office at the UW. Paper field notes maintained by Community Health Workers may be scanned and emailed from the local health clinics to UW using YKHC scanners or collected by UW study staff and hand carried from the field research sites to the UW. All original paper documents will be maintained by the CHW in lockable cases that can be moved from place to place. As soon as CHWs have scanned and emailed original documents to UW the original documents will be stored in the lockable cases. In case of remote delivery of the intervention, paper study forms will only be used in case of Internet outages.

All survey data (demographic, fruit drink, food, hair, beverage questionnaire, adverse events) will be captured electronically on a laptop that has a secure REDCap database installed or will be entered onto REDCap by UW study staff while the participant answers questions over the phone. The laptop will be password protected and will only be used by study staff. The laptop will remain with staff while in the field and will be transported to UW at the end of visits to the communities. Data will be uploaded onto secure servers at UW when Wi-Fi access is available. Alternately all data collection may be conducted remotely due to Covid-19 restrictions.

The 24-hour food recall data will be collected electronically by a study staff member in person or via phone/video call using the University of Minnesota's Nutrition Data System for Research (NDSR) on password-protected study laptops. NDSR files will be shared with study personnel using secure, password-protected servers. Study staff will have ways to back up NDSR data and will carry paper data collection forms in case of laptop failures. In case of remote study delivery there will be no need for paper forms.

Plaque samples will be identified by study ID only and will be hand carried to UW by trained study staff and stored according to manufacturer instructions. Hair samples will be identified by study ID only and will be hand carried to UW by trained study staff and then mailed to UAF for processing and biomarker analysis. The hair is destroyed during the processing and biomarker data will be stored on secure, password-protected servers. Data will be transferred from UAF to UW via secure FTP. As noted, in case of remote delivery of the study plaque samples will not be collected and hair samples will be self-collected by study participants.

All qualitative data (e.g., 6-month and 12-month post-intervention interview with caregivers) will be audio recorded. Recordings will be protected from disclosure by uploading digital files onto password-protected study laptops. These files will be transmitted electronically to secure servers at the UW and stored on secure, password-protected servers. All transcribed data will be stored on secure, password-protected servers at the UW, which only members of the study team having a role in data analysis will have access to.

17.2 Types of Data

There are multiple types of data that will be collected including demographic, behavioral, biomarker, food, diet, weight, safety, and interview data.

17.3 Schedule and Content of Reports

Weekly reports will be generated to monitor enrollment and monthly reports to summarize study progress (enrollment, intervention visits completed, data collection points completed). The final data analysis will be completed within 3 months of having all the necessary study variables. The statistician will be masked on whether the community is in the intervention vs. comparison group.

17.4 Study Records Retention

Study records will be maintained for at least 3 years from the date that the last grant federal financial report is submitted to the NIH.

17.5 Protocol Deviations

A protocol deviation is any noncompliance with the clinical study protocol or Good Clinical Practice requirements. The noncompliance may be on the part of the participant, the investigator, or study staff. As a result of deviations, corrective actions are to be developed by the study staff and implemented promptly.

These practices are consistent with investigator and sponsor obligations in ICH E6.

All deviations from the protocol must be addressed in study participant source documents and will be reported to the IRB and NIDCR, according to their requirements, at the agreed upon timeframe.

PUBLICATION/DATA SHARING

Before disseminating our study findings to the scientific community at research conferences and peer-reviewed journals, all study findings will be reviewed by the Yukon-Kuskokwim Health Corporation's Human Studies Committee. Any publications, abstract, or presentations involving data from this study must be approved in writing by the YKHC. The YKHC requires at least 60 days advanced notice to review reports, manuscripts, and conference abstracts. Research results will be submitted to the YKHC Board for review before we make them public in professional journals, other news media, or presentations. When research results are reported in a professional setting, such as in a peer-reviewed journal or at a scientific meeting, the identity of individual research participants and their communities will not be disclosed. We agree to provide appropriate acknowledgement of YKHC as the source of the data in all appropriate published or oral communications involving the research project. This is a mandatory step prior to any public dissemination of research findings related to local Yup'ik populations. Next, study findings will be shared with local communities, including Tribal Council and local community meetings.

This study will comply with all applicable NIH Data Sharing Policies. See https://grants.nih.gov/policy/sharing.htm for policies and resources.

18.0 NIH Public Access Policy

The NIH Public Access Policy requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to PubMed Central immediately upon acceptance for publication. This ensures that the public has access to the published results of NIH funded research.

18.1 NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information

The study is a clinical trial and will comply with the NIH policy that establishes the expectation that all investigators conducting clinical trials funded in whole or in part by the NIH will ensure that these trials are registered at ClinicalTrials.gov, and that results of these trials are submitted to ClinicalTrials.gov.

LITERATURE REFERENCES

Bandura A. Social cognitive theory: an agentic perspective. Annu Rev Psychol. 2001;52:1-26.

Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. J Pers Soc Psychol T. 1986;51(6):1173-82.

Batliner T, Wilson AR, Tiwari T, Glueck D, Henderson W, Thomas J, Braun P, Cudeii D, Quissell D, Albino J. Oral health status in Navajo Nation Head Start children. J Public Health Dent. 2014;74(4):317-25.

Chi DL, Coldwell SE, Mancl L, Hopkins S, Senturia K, Randall CL, Orr E, Cruz S. Alaska Native Children Do Not Prefer Sugar-Sweetened Fruit Drinks to Sugar-Free Fruit Drinks. J Acad Nutr Diet. 2019;119(6):984-990.

Chi DL, Hopkins S, O'Brien D, Mancl L, Orr E, Lenaker D. Association between added sugar intake and dental caries in Yup'ik children using a novel hair biomarker. BMC Oral Health. 2015;15(1):121.

Ebbeling CB, Feldman HA, Chomitz VR, Antonelli TA, Gortmaker SL, Osganian SK, Ludwig DS. A randomized trial of sugar-sweetened beverages and adolescent body weight. N Eng J Med. 2012;367:1407-1416.

Eldridge SM, Ashby D, Kerry S. Sample size for cluster randomized trials: effect of coefficient of variation of cluster size and analysis method. Int J Epidemiol. 2006:35;1292-1300.

Fitch C, Keim KS; Academy of Nutrition and Dietetics. Position of the Academy of Nutrition and Dietetics: use of nutritive and nonnutritive sweeteners. J Acad Nutr Diet. 2013;112(5):739-58.

Gittelsohn J, Rowan M, Gadhoke P. Interventions in small food stores to change the food environment, improve diet, and reduce risk of chronic disease. Prev Chronic Dis. 2012;9:E59.

Hardin JW, Hilbe JM. Generalized Estimating Equations. New York: Chapman & Hall/CRC, 2003.

Hayes AF. Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach. 2013, New York: Guilford.

Institute of Medicine (IOM). 2002/2005. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids / Panel on

Macronutrients, Panel on the Definition of Dietary Fiber, Subcommittee on Upper Reference Levels of Nutrients, Subcommittee on Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board. Washington, DC: IOM.

James J, Thomas P, Cavan D, Kerr D. Preventing childhood obesity by reducing consumption of carbonated drinks: clustered 59andomized controlled trial. Br Med J. 2004;328:1237-1239.

Magnuson BA, Carakostas MC, Moore NH, Poulos SP, Renwick AG. Biological fate of low-calorie sweeteners. Nutr Rev. 2016;74(11):670-689.

Magnuson BA, Roberts A, Nestmann ER. Critical review of the current literature on the safety of sucralose. Food Chem Toxicol. 2017;106(Pt A):324-355.

Nash SH, Kristal AR, Hopkins SE, Boyer BB, O'Brien DM. Stable isotope models of sugar intake using hair, red blood cells, and plasma, but not fasting plasma glucose, predict sugar intake in a Yup'ik study population. J Nutr. 2014;144(1):75-80.

Nash SH, Kristal AR, Bersamin A, Hopkins SE, Boyer BB, O'Brien DM. Carbon and nitrogen stable isotope ratios predict intake of sweeteners in a Yup'ik study population. J Nutr. 2013;143(2):161-5.

Rotnizky A, Robins JM, Scharfstein DO. Semiparametric regression for repeated outcomes with nonignorable nonresponse. J Am Stat Assoc. 1998;93:1321-1339.

Schafer JL. Analysis of Incomplete Multivariate Data. New York, NY: Springer-Verlag; 2005.

Sheiham A, James WP. A new understanding of the relationship between sugars, dental caries and fluoride use: implications for limits on sugars consumption. Public Health Nutr. 2014;17(10):2176-84.

Sichieri R, Trotte AP, de Souza RA, Veiga GV. School 59andomized trial on prevention of excessive weight gain by discouraging students from drinking sodas. Public Health Nutr. 2008;12:197-202.

Singh AS, Paw M, Brug J, van Mechelen W. Dutch obesity intervention in teenagers effectiveness of a school-based program on body composition and behavior. Arch Pediatr Adolesc Med. 2009;163:309-317.

Sylvetsky AC, Jin Y, Clark EJ, Welsh JA, Rother KI, Talegawkar SA. Consumption of Low-Calorie Sweeteners among Children and Adults in the United States. J Acad Nutr Diet. 2017;117(3):441-448.e2.

Sylvetsky AC, Rother KI. Nonnutritive Sweeteners in Weight Management and Chronic Disease: A Review. Obesity (Silver Spring). 2018;26(4):635-640.

Vos MB, Kaar JL, Welsh JA, Van Horn LV, Feig DI, Anderson CAM, Patel MJ, Cruz Munos J, Krebs NF, Xanthakos SA, Johnson RK; American Heart Association Nutrition Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Clinical Cardiology; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Epidemiology and Prevention; Council on Functional Genomics and Translational Biology; and Council on Hypertension. Added Sugars and Cardiovascular Disease Risk in Children: A Scientific Statement From the American Heart Association. Circulation. 2017 May 9;135(19):e1017-e1034.

APPENDICES

APPENDIX A: SCHEDULE OF EVENTS

Procedures	Screening (Day –30 to –1)	Baseline Visit 1 (Day 0)	Study Visit 2 (before 1m data)	Study Visit 3 (before 1m data)	Study Visit 4 (Day 30 + 7 days)	Study Visit 5 (before 3m data)	Study Visit 6 (before 3m data)	Study Visit 7 (before 3m data)	Study Visit 8 (Day 90 ± 7 days)	Study Visit 9 (before 6m data)	Study Visit 10 (before 6m data)	Study Visit 11 (before 6m data)	Study Visit 12 (before 6 months	Study Visit 13 (Day180±30days)	Study Visit 14 (Day 360±30days)
Signed Consent and Assent	X														X**
Assessment of Eligibility Criteria	X	X													X**
Study Intervention			X	X		X	X	X		X	X	X	X		
Other Procedures: Demographic data		X													
Other Procedures: Fruit drink survey		X			X				X					X	X
Other Procedures: 24-hour food recall data*, food survey*, hair survey, beverage questionnaire		X			X				X					X	X
Plaque sample from child		X			X				X					X	X
Hair sample from child and caregiver (about 20 strands)		X			X				X					X	X
Side effects and adverse events					X	X	X	X	X	X	X	X	X	X	X
Other Procedures: Qualitative intervention feedback interview														X	X

*Optional at Study Visit 8 (3m), Study Visit 13 (6m), and Study Completion (12m)

** For interested families in the control group only

Procedures	Control Study Visit 15 (before 3m data)	Control Study Visit 16 (before 3m data)	Control Study Visit 17 (before 3m data)	Control Study Visit 18 (before 3m data)	Control Study Visit 19 (before 3m data)	Control Study Visit 20 (before 3m data)	Control Study Visit 21 3m data collection visit	Control Study Visit 22 6m data collection visit
Signed Consent and Assent	X							
Assessment of Eligibility Criteria	X							
Study Intervention	X	X	X	X	X	X		
Other Procedures: Demographic data							X	X
Other Procedures: Fruit drink survey							X	X
Other Procedures: 24-hour food recall data*, food survey*, hair survey							X	X
Plaque sample from child							X	X
Hair sample from child and caregiver (about 20 strands)							X	X
Side effects and adverse events							X	X
Other Procedures: Qualitative intervention feedback interview							X	X

*Optional at Study Visit 14

APPENDIX B: DEMOGRAPHIC SURVEY (ADULT)

The following questions are about you and your family

How old are you?

_____

What is your sex?

- ◯ Male
- ◯ Female

How many children are in your household?

_____

How many people currently live in your household (including yourself)

_____

What is the estimated total Annual Income of all people in your household, including any subsidies like energy relief, or general assistance?

- ◯ less than $10,000
- ◯ $10,000~$14,999
- ◯ $15,000~$24,999
- ◯ $25,000~$34,999
- ◯ $35,000~$49,999
- ◯ $50,000~$74,999
- ◯ $75,000~$99,999
- ◯ Refused/Did not wish to answer

How often does your money for household utilities (i.e. water, fuel oil, electricity, etc.) run out before the end of the month?

◯ Never ◯ Seldom ◯ Sometimes ◯ Most times ◯ Always ◯ Refused/Did not wish to answer

What is the primary language spoken in your home?

- ◯ Yu'pik only
- ◯ English only
- ◯ Both Yu'pik and English

People talk to us about the traditional ways of living. How much do you follow the traditional Yup'ik way of life?

- ◯ A lot
- ◯ Sometimes
- ◯ Rarely
- ◯ Never

APPENDIX C: DEMOGRAPHICS SURVEY (CHILD)

Demographics (child)

This survey is about the children in your household. You will be asked to repeat the survey for each child. Please answer all the questions for each child.

Thank you!

For the Interviewer **New Study ID for the Child**	
This is the adult person's study ID number with site variable added (No Action Needed - Please Note on Specimen Log Sheets)	_____
Child Number (Please indicate with 2 numbers. For example, the first or oldest child in the household would be 01, next child would be 02, next 03, etc.)	_____
This is the child's study ID. Please add the child number to the end of the Adult Study ID (e.g., "child number": 01, "adult study ID": 210, "child study ID": 21001)	_____
Today's Date	_____

APPENDIX D: STRUCTURED VISIT FORM

Structured Visit Form (CHW)

Please complete this form after you have completed the home visit.

Thank you!

Home Visit Log

Today's date _____

Name of Community Health Worker
- ◯ Andrea Dock
- ◯ Deanna Wiseman
- ◯ Diane Atti

Home visit number
- ◯ Home visit 1 - health education (SV 2)
- ◯ Home visit 2 - health education (SV 3)
- ◯ Home visit 3 - self efficacy (SV 5)
- ◯ Home visit 4 - self efficacy (SV 6)
- ◯ Home visit 5 - self efficacy (SV 7)
- ◯ Home visit 6 - check in (SV 9)
- ◯ Home visit 7 - check in (SV 10)
- ◯ Home visit 8 - check in (SV 11)
- ◯ Home visit 9 - check in (SV 12)

What time did you arrive at the home? _____

What time did you leave the home? _____

Checklist for each study visit (completed by the Community Health Worker)

	Yes	No	Not applicable
Caregiver was available to make a study appointment	◯	◯	◯
Caregiver was ready for study appointment at the agreed upon date and time	◯	◯	◯
Study appointment had to be rescheduled by the caregiver	◯	◯	◯
(All) enrolled child(ren) present	◯	◯	◯
Caregiver completed assignment ahead of time	◯	◯	◯
Home was too loud during visit	◯	◯	◯
Caregiver appeared distracted (using cell phone, cooking, other)	◯	◯	◯
Was able to complete all study visit tasks	◯	◯	◯

Number of scheduling attempts made before study visit took place _____

Other problems _____

Field notes from visit _____

Any other notes _____

APPENDIX E: FRUIT DRINK SURVEY

(Please read to caregiver)

We are going to be talking about sugared fruit drinks: the kinds of drinks where you add a powdered mix to water. We will use Tang and Kool-Aid as examples of sugared fruit drinks, which could also include drinks like Hawaiian Punch and Country Time Lemonade. Keep in mind that we are not talking about soda pop or the warm Tang you give to your child when he/she is sick. For each statement, please choose whether you strongly agree, agree, have no opinion, disagree, or strongly disagree.

Section 1

	Strongly agree	Agree	No opinion	Disagree	Strongly disagree
Tang and Kool-Aid are healthy for my child. [in general]	○	○	○	○	○
It is important to limit how much Tang and Kool-Aid my child drinks.	○	○	○	○	○
Watering down Tang and Kool-Aid makes them healthier. [adding more water than the package says so it's diluted]	○	○	○	○	○
Preventing cavities is important.	○	○	○	○	○
It is important for me to help my child to be cavity-free.	○	○	○	○	○
Sugar-free drinks are unsafe	○	○	○	○	○

[Present photo of sugar-free Tang and Kool-Aid to participants and say]: Here is a picture of sugar-free Tang and Kool-Aid.

Tang and Kool-Aid

Sugar-free Tang and Kool-Aid

Have you seen these drinks before? ○ Yes ○ No

Here are some more statements regarding sugar-free Tang and Kool-Aid. Please answer whether you strongly agree, agree, have no opinion, disagree, or strongly disagree.

Section 1A

	Strongly Agree	Agree	No opinion	Disagree	Strongly Disagree
Sugar-free Tang and Kool-Aid are healthier than regular Tang and Kool-Aid.	○	○	○	○	○
Sugar-free Tang and Kool-Aid are not as tasty as regular Tang and Kool-Aid.	○	○	○	○	○

The following statements are related to supervising/controlling your child's drink intake. For the following statements, please choose whether you strongly agree, agree, have no opinion, disagree, or strongly disagree.

Section 2

	Strongly agree	Agree	No opinion	Disagree	Strongly disagree
I can get my child to drink less regular Tang and Kool-Aid	○	○	○	○	○
I can get my child to drink sugar-free Tang and Kool-Aid	○	○	○	○	○

The following statements are related to products you see in the store. For the following, please answer whether the statements are often, sometimes, or never true.

Section 3

	Often	Sometimes	Never
Sugar-free Tang and Kool-Aid are available in my village	○	○	○
Crystal Light is available in my village	○	○	○
Other adults in my home, like grandparents or relatives, give my child regular Tang and Kool-Aid	○	○	○

The following statements are about Tang and Kool-Aid. For the following statements, please choose whether you believe each statement is true or false.

Section 4

	True	False
Tang and Kool-Aid contain vitamin C	○	○
Tang and Kool-Aid are healthier than soda pop	○	○
Sugar-free Tang and Kool-Aid lead to cavities in children	○	○

As a reminder, sugared fruit drinks include Tang, Kool-Aid, Hawaiian Punch, Country Time Lemonade, and other kinds of drinks where you add a powdered mix to water. Do you give your child sugared fruit drinks?	○ Yes ○ No

(Staff - Please skip this section if the parent says no to the previous question. No questions will appear if they said no.)

Below are some reasons parents give their child sugared fruit drinks. Please tell me which apply to you. You can answer with a "Yes" or "No". You can answer yes to as many as you think apply to you.

(Staff - Please repeat the phrase "Parents give their child sugared fruit drinks..." before each statement)

Section 5

	Yes	No
Because they are a good replacement for fruits, like oranges and grapes	○	○
Because they are a good treat for my child	○	○
Because they are inexpensive or cheap	○	○
Because they make my child happy	○	○
Because others in my village drink them	○	○
Because they are healthier than soda pop	○	○
Because there are few other drinks that I can give my kids	○	○
Because they are what I grew up with	○	○
Because they are part of being a child	○	○

What are some other reasons you give your child regular Tang and Kool-Aid?

_____

As a reminder, examples of sugar-free fruit drinks are Crystal Light, sugar-free Tang, and sugar-free Kool-Aid. Do you give your child sugar-free drinks?

○ Yes
○ No

(Staff - Please skip this section if the parent says no to the previous question. No questions will appear if they said no.)

Below are some reasons parents give their child sugar-free fruit drinks. Please tell me which apply to you. You can answer with a "Yes" or "No". You can answer yes to as many as you think apply to you.

(Staff - Please repeat the phrase "Parents give their child sugar-free fruit drinks... before each statement.)

Section 6

	Yes	No
Because they are a good replacement for fruits like oranges and grapes	○	○
Because they are a good treat for my child	○	○
Because they are inexpensive or cheap	○	○
Because they make my child happy	○	○
Because others in my village drink them	○	○
Because they are healthier than soda pop	○	○
Because they are part of being a child	○	○

What are some other reasons you give your child sugar-free drinks? _____

APPENDIX F: PAPER VERSION OF FRUIT DRINK SURVEY

REDUCING SUGARED FRUIT DRINKS IN ALASKA NATIVE CHILDREN
FRUIT DRINK SURVEY
SEPTEMBER 2023
[«SURVEY_»][«MATCH_ID»]

This section is to be completed by UW Study staff.

DATE:____/____/_____ TIME:_____ COMMUNITY: «COMMUNITY»

Household ID: «HOUSEHOLD_ID» Caregiver ID:_____ Child ID: «CHILD_ID» Combined ID:_____

Please answer the questions on this form for this child [*CHILD NAME: «FULL_NAME»*]

What is your relationship to this child [«FIRST_NAME»]?						
Please circle one.						
Mother	Father	Grandmother	Grandfather	Aunt	Uncle	Other

These questions are about sugared fruit drinks. The kind where you add a powdered mix to water like Tang and Kool-Aid.

Keep in mind that we are not asking about soda-pop or the warm tang you may give your child when he/she is sick.

For each of the following, please circle one response.					
Tang and Kool-Aid are healthy for my children, in general.	Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
It is important to limit how much Tang and Kool-Aid my children drink.	Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
Preventing cavities is important.	Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
It is important for me to help my children to be cavity-free.	Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
Sugar-free drinks are unsafe.	Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree

Quyana for your responses!

Page **1** of **4**

REDUCING SUGARED FRUIT DRINKS IN ALASKA NATIVE CHILDREN
FRUIT DRINK SURVEY
SEPTEMBER 2023
[«SURVEY_»][«MATCH_ID»]

Have you seen these drinks before?	
Tang and Kool-Aid  **Sugar-free Tang and Kool-Aid** 	*Please circle one.* **YES** **NO**

These statements are about supervising/controlling your child's drink intake.					
For each of the following, please circle one response.					
I can get [«FIRST_NAME»] to drink less regular Tang and Kool-Aid.	Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
I can get [«FIRST_NAME»] to drink sugar-free Tang and Kool-Aid.	Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree

Quyana for your responses!

REDUCING SUGARED FRUIT DRINKS IN ALASKA NATIVE CHILDREN
FRUIT DRINK SURVEY
SEPTEMBER 2023
[«SURVEY_»][«MATCH_ID»]

The following statements are related to products you see in the store.			
For each of the following, please circle one response.			
Sugar-free Tang and Kool-Aid are available in my village.	**Often**	**Sometimes**	**Never**
Crystal Light is available in my village.	**Often**	**Sometimes**	**Never**
Other adults in my home, like grandparents or relatives, give my child regular Tang and Kool-Aid.	**Often**	**Sometimes**	**Never**

The following statements are about Tang and Kool-Aid.		
For each of the following, please circle one response.		
Tang and Kool-Aid contain vitamin C.	**True**	**False**
Tang and Kool-Aid are healthier than soda pop.	**True**	**False**
Sugar-free Tang and Kool-Aid lead to cavities in children.	**True**	**False**

As a reminder, sugared fruit drinks include Tang, Kool-Aid, Hawaiian Punch, Country Time Lemonade, and other kinds of drinks where you add a powdered mix to water.		
Please circle one response.		
Do you give [«FIRST_NAME»] sugared fruit drinks?	**Yes**	**No**

Quyana for your responses!

REDUCING SUGARED FRUIT DRINKS IN ALASKA NATIVE CHILDREN
FRUIT DRINK SURVEY
SEPTEMBER 2023
[«SURVEY_»][«MATCH_ID»]

Below are some reasons parents give their child sugared fruit drinks.		
For each of the following, please circle one response if it applies to you and **[«FIRST_NAME»]**.		
Parents give their child sugared fruit drinks **because they are a good replacement for fruits, like oranges and grapes.**	**Yes**	**No**
Parents give their child sugared fruit drinks **because they are a good treat for my child.**	**Yes**	**No**
Parents give their child sugared fruit drinks **because they are inexpensive or cheap.**	**Yes**	**No**
Parents give their child sugared fruit drinks **because they make my child happy.**	**Yes**	**No**
Parents give their child sugared fruit drinks **because others in my village drink them.**	**Yes**	**No**
Parents give their child sugared fruit drinks **because they are healthier than soda pop.**	**Yes**	**No**
Parents give their child sugared fruit drinks **because there are few other drinks that I can give my kids.**	**Yes**	**No**
Parents give their child sugared fruit drinks **because they are what I grew up with.**	**Yes**	**No**
What are some other reasons you give [«FIRST_NAME»] regular Tang and Kool-Aid?		
Please write your response below.		

Quyana for your responses!

Page **4** of **4**

APPENDIX G: FOOD SURVEY

Please read the following questions to the Caregiver	
How often does your money for food run out before the end of the month?	◯ Never ◯ Seldom ◯ Sometimes ◯ Most times ◯ Always
In the past 12 months, the food you bought just didn't last, and you didn't have money to get more. Is this statement always, sometimes, or never true?	◯ Always True ◯ Sometimes True ◯ Never True
In the past 12 months, you worried whether your food would run out before you got money to buy more. Is this statement always, sometimes, or never true?	◯ Always True ◯ Sometimes True ◯ Never True
Do you receive assistance to pay for food (i.e., food stamps or WIC coupons)?	◯ Yes ◯ No
How much of your child's home diet consists of eating traditional Alaska Native foods?	◯ A lot ◯ Sometimes ◯ Rarely ◯ Not at all
How much does your household eat traditional Alaska Native foods?	◯ A lot ◯ Sometimes ◯ Rarely ◯ Not at all
Please specify how much traditional Alaska Native food each child consumes.	_____
What percentage of your first child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____
What percentage of your second child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____
What percentage of your third child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____
What percentage of your fourth child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____
What percentage of your fifth child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____
What percentage of your sixth child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____

What percentage of your seventh child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____
What percentage of your eighth child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____
What percentage of your ninth child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____
What percentage of your tenth child's home-based caloric intake consists of Alaska Native foods? (0%-100%)	_____
Are you currently breastfeeding or feeding pumped milk to a new baby?	◯ Yes ◯ No ◯ Not applicable
Does your child spend most of their time living with you (more than half the time)?	◯ Yes ◯ No

APPENDIX H: HAIR SURVEY (CAREGIVER)

Hair Survey (caregiver)

Please complete all the information about the caregiver.

For staff use only	
Today's Date	_____
Name of staff collecting hair sample	◯ Donald Chi ◯ Anna Tourovskaia ◯ Cameron Randall ◯ Alice Ko ◯ Joshua Orack
Hair type	◯ Long ◯ Short

Please read the following questions to the Caregiver	
Is your hair currently colored?	◯ Yes ◯ No
Is all of your hair colored or just sections?	◯ All ◯ Just Sections
Which type of hair coloring products did you use?	◯ Bleach ◯ Permanent hair dye ◯ Semi-permanent or temporary hair dye ◯ Wash out hair dye

APPENDIX I: HAIR SURVEY (CHILD)

Hair Survey (child)

Please complete for each child.

For staff use only

Today's Date

_____

Name of staff collecting hair sample

- ◯ Donald Chi
- ◯ Anna Tourovskaia
- ◯ Cameron Randall
- ◯ Alice Ko
- ◯ Joshua Orack

Child's Study ID Number

_____

Hair type

- ◯ Long
- ◯ Short

Weight (lbs)

_____

Please read the following questions for the Caregiver

Is your child's hair currently colored?

- ◯ Yes
- ◯ No

Is all of your child's hair colored or just sections?

- ◯ All
- ◯ Just sections

Which hair coloring products were used by your child?

- ◯ Bleach
- ◯ Permanent hair dye
- ◯ Semi-permanent or temporary hair dye
- ◯ Wash-out hair dye

APPENDIX J: SIDE EFFECTS AND ADVERSE EVENTS FORM

Page 1

Side Effects and Adverse Events

Please answer the following questions about any adverse effects you may have experienced.

For the Interviewer	
Today's date	_____
Was this a home visit or a clinic visit?	◯ Home visit ◯ Clinic visit
What home visit number was this?	◯ Home visit 1 - health education (SV 2) ◯ Home visit 2 - health education (SV 3) ◯ Home visit 3 - self efficacy (SV 5) ◯ Home visit 4 - self efficacy (SV 6) ◯ Home visit 5 - self efficacy (SV 7) ◯ Home visit 6 - check in (SV 9) ◯ Home visit 7 - check in (SV 10) ◯ Home visit 8 - check in (SV 11) ◯ Home visit 9 - check in (SV 12)

(Please read to caregiver)
The following questions are regarding any adverse incidents that may have happened since the last time we visited. Please answer any or all questions that you and your children experienced.

Since the last time we visited, has your child or anyone in your family had or currently have an upset stomach, runny stool, or diarrhea?	◯ Yes ◯ No
Which of the following did your child have? Select all that apply.	☐ Upset Stomach ☐ Runny Stool ☐ Diarrhea ☐ Other
Please specify what type of side effect your child experienced.	_____
How bad was the side effect(s)?	◯ Mild ◯ Moderate ◯ Severe
What do you think the reason was for this side effect?	_____
What made it better?	_____
Do you think this was related to the sugar-free fruit drinks?	◯ Yes ◯ No
Who mixed the sugar-free drinks?	_____
Did the person who mixed the sugar-free drinks follow the study instructions?	◯ Yes ◯ No ◯ I don't know
Was the container of sugar-free mix stored out of reach of children?	◯ Yes ◯ No ◯ I don't know
Did an adult supervise your child's intake of the sugar-free drink?	◯ Yes ◯ No ◯ I don't know
Did the child get more sugar-free drink than the card recommends?	◯ Yes ◯ No ◯ I don't know
How much more than the card recommendation did your child drink?	_____

APPENDIX K: ADULT CONSENT FORM (INTERVENTION ARM)

Study Participation Consent & Parental Permission Form: Intervention Arm

Reducing Sugared Fruit Drinks in Alaska Native Children

Main Researchers: Dr. Donald Chi, Professor, University of Washington, School of Dentistry, Department of Oral Health Sciences, 206-616-4332

Researchers' Statement

We are asking you and your child to be in a research study. The purpose of this consent form is to give you the information you'll need to help you decide if you want to be in the study or not. Please read the form carefully. You may ask any questions about the research or this form. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called "informed consent." We will give you a copy of this form for your records.

PURPOSE OF THE STUDY

The study goal is to learn if a community program can help Yup'ik children to drink less sugary drinks and have fewer cavities. In the study, participants will be assigned into either an intervention community (receive the program first) or a control community (receive the program later). Your community has been assigned to the intervention community. That means you will receive the program first.

STUDY PROCEDURES

The study will last about one year. We will ask you and your child to join us at the Community Clinic 5 times. A trained staff person will ask you questions about your children's diet, measure your child's weight, use scissors to cut about 20 strands of hair from yourself and your child and collect an oral plaque specimen using a swab. Each visit will last up to 1 and 1/2 hours. You will receive a $25 store gift card per child after completing each visit. If you and your child make all 5 visits, you will receive a $50 bonus gift card for each child after the last visit. At the 4th and 5th visit, we will ask for your feedback about the health program. We would like to audio record the conversations if that is okay with you. You can review transcripts of the conversations if you would like.

In addition, a trained Community Health Worker (CHW) will contact you and your child 9 times during the 6-month study period. Each visit will last 5 to 30 minutes, for about 2-3 hours total. In the first visit, we will show information about fruit drinks and cavities. In the second visit, we will introduce sugar-free drinks by sending you supplies in the mail. During the third to fifth visits, we will work with you to improve ways to get your child to accept healthier drinks. After that, there will be four 5-minute check-ins to see your progress in the program. In case there is a COVID-19 risk at the time of these visits, the CHW will either conduct the visits entirely by Internet using a tablet or will visit your home using a mask and other precautions such as social distancing.

RISKS, STRESS, OR DISCOMFORT

You may feel uncomfortable participating in our study in some situations. First, in some cases, when children have too many sugar-free fruit drinks, they might have an upset tummy or runny stool. These side effects may also occur in adults. Sugar-free fruit drinks are FDA-approved and safe for children when they drink the right amount. To be safe, families who participate in our program should follow the mixing instructions. Caregivers need to keep an eye on the number of sugar-free drinks they and their child have.

Second, there is a chance that other community members may be aware of your participation in our study. That may make you feel uncomfortable. However, your personal information will be securely stored. We will not share your information with anyone besides our study staff.

Third, you and your children may feel uncomfortable about providing your weight, hair and oral plaque samples. You may also feel uncomfortable sharing what your children ate. If you or your children feel any discomfort, you may stop participating at any time. Your decision will not change the care that you and your child receive from YKHC. You and your child may say no to any part of the study. You and your child are free to drop off from this study at any time without penalty or loss of your current benefits.

BENEFITS OF THE STUDY

Direct benefits include receiving oral health information and counseling. You will also receive free sugar-free drink samples. You and your child may or may not experience a direct health benefit. However, by switching sugared-fruit drinks to sugar-free fruit drinks, we expect your child to have less sugar intake and cavities.

SOURCE OF FUNDING

The study is funded by the National Institutes of Health.

CONFIDENTIALITY OF RESEARCH INFORMATION

Information about this study will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. You can search this Web site at any time.

You and your children's information are confidential. The samples and information you and your child provide will be stored with only an identification number. Your and your child's name will not appear on the samples and information. Only de-identified information and samples will be provided to the researcher doing the analysis. Your name on the consent form will be kept separate from the information you provide for the study. Identifying information will be stored in locked file cabinets at the University of Washington.

We submit research findings to the YKHC Board for review and approval before we make them public in professional journals, other news media, or presentations. When research findings are reported in a professional setting, such as in a medical journal or at a scientific meeting, we will not identify you and your community.

We have a Certificate of Confidentiality from the federal National Institutes of Health. This helps us protect your privacy. The Certificate means that we do not have to give out identifying information about you even if we are asked to by a court of law. We will use the Certificate to resist any requests for identifying information.

We can't use the Certificate to withhold your research information if you give your written consent to give it to an insurer, employer, or other person. Also, you or a member of your family can share information about yourself or your part in this research if you wish.

There are some limits to this protection. We will voluntarily provide the information to:

- a member of the federal government who needs it in order to audit or evaluate the research;
- individuals at the University of Washington, the funding agency, and other groups involved in the research, if they need the information to make sure the research is being done correctly;
- the FDA, if required by the FDA;
- state or local authorities, if we learn of child abuse, elder abuse, or the intent to harm yourself or others.

The Certificate expires when the NIH funding for this study ends. Currently this is March 31, 2023. Any data collected after expiration is not protected, as described above. Data collected prior to expiration will continue to be protected.

Government or university staff sometimes review studies to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

USE OF INFORMATION AND SPECIMENS

The information you provide in this study may be used for future research studies related to oral health. It is also possible that in the future we may want to use or share study information that might identify you. If we do, we will obtain additional consent from you at that time.
You and your child's hair and oral plaque samples belong to you. These samples will be stored at UW and UAF. All the samples are stored with only an identification number. Your and your child's name will not appear on your samples. Analyses of your hair samples will be conducted under the direction of Dr. Diane O'Brien, our collaborator on this project. Plaque samples will be stored at UW in a secure freezer for analysis at a later date. This research does not involve giving treatment or other medical care as a part of the study. It only involves using this information to better understand sugar intake and cavities among Alaska Native children. You and your child's hair samples will be destroyed after analysis; there will not be any remaining unused sample. The information that we obtain from you and your child's hair and plaque samples will not have any identifying information.

We would like to store your child's plaque samples for future analyses. We want to know if the program changed the types of bacteria in your child's mouth. The reason we are storing the samples

is that we currently do not have funding to analyze the plaque samples. Regardless of future analyses, all plaque specimens collected will be destroyed by 2027. If you don't want your child's plaque samples stored, they can still be in the study. It will not change their participation. You may ask to have your child's samples removed from our freezers at any time. Call Dr. Donald Chi, at 206-616-4332.

☐ I agree to have my child's plaque samples stored for future analyses.

Participant Initials:_____

☐ I DO NOT agree to have my child's plaque samples stored for future analyses.

RESEARCH-RELATED INJURY

If you think you have been harmed from being in this research, contact Dr. Donald Chi at 1-206-616-4332 or e-mail him at dchi@uw.edu or Dr. Joseph Klejka, YKHC Vice President of Quality, in Bethel at (907) 543-6028.

Printed name of study staff obtaining consent Signature Date

Participant's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research participant, I can call the University of Washington Human Subjects Division at (206) 543-0098 or call collect at (206) 221-5940. I will receive a copy of this consent form.

Printed name of participant Signature of participant
Date

Home address Phone number

Printed name of Yup'ik translator Signature of translator Date

Copies to: Researcher | Participant

APPENDIX L: ADULT CONSENT FORM (CONTROL)

Study Participation Consent & Parental Permission Form: Control Arm

Reducing Sugared Fruit Drinks in Alaska Native Children

Main Researchers: Dr. Donald Chi, Professor, University of Washington, School of Dentistry, Department of Oral Health Sciences, 206-616-4332

Researchers' Statement

We are asking you and your child to be in a research study. The purpose of this consent form is to give you the information you'll need to help you decide if you want to be in the study or not. Please read the form carefully. You may ask any questions about the research or this form. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called "informed consent." We will give you a copy of this form for your records.

PURPOSE OF THE STUDY

The study goal is to learn if a community program can help Yup'ik children to drink less sugary drinks and have fewer cavities. In the study, participants assigned into either an intervention community (receive the program first) or a control community (receive the program later). Your community has been assigned to the control community. That is, you and your child will not receive the program at first. But will have the option to receive the program at the end of the study. This way, we can see if the program worked.

STUDY PROCEDURES

The study will last about one year. We will ask you and your child to join us for a meeting at the Community Clinic 5 times. A trained staff person will ask you questions about your children's diet, measure your child's weight, use scissors to cut about 20 strands of hair from yourself and your child and collect an oral plaque specimen using a swab. Each visit will last up to 1 and 1/2 hours. You will receive a $25 store gift card per child after completing each visit. If you and your child make all 5 phone visits, you will receive a $50 bonus gift card for each child after the last visit.

At the end of the study, you and your child will have the option to receive the program. A trained Community Health Worker (CHW) will visit you and your child 9 times during the 6-month study period. Each visit will last 5 to 30 minutes, with about 2-3 hours total. In the first visit, we will show information about fruit drinks and cavities. In the second visit, we will introduce sugar-free drinks. During the third to fifth visits, we will work with you to improve ways to get your child to accept healthier drinks. After that, there will be 4, 5-minute check-ins to see your progress in the program. In case there is a Covid-19 risk at the time of these visits, the CHW will either conduct the visits entirely by internet using a tablet or will visit your home using a mask and other precautions such as social distancing. .

RISKS, STRESS, OR DISCOMFORT

You may feel uncomfortable participating in our study in some situations. First, in some cases, when children have too many sugar-free fruit drinks, they might have an upset tummy or runny

stool. These side effects may occur in adults as well. Sugar-free fruit drinks are FDA-approved and safe for children when they drink the right amount. To be safe, families who participate in our program should follow the mixing instructions. Caregivers need to keep an eye on the number of sugar-free drinks they and their child have.

Second, there is a chance that other community members may be aware of your participation in our study. That may make you feel uncomfortable. However, your personal information will be securely stored. We will not share your information with anyone besides our study staff.

Third, you and your children may feel uncomfortable about providing your weight, hair and oral plaque samples. You may also feel uncomfortable sharing what your children ate. If you or your children feel any discomfort, you may stop participating at any time. Your decision will not change the care that you and your child receive from YKHC. You and your child may say no to any part of the study. You and your child are free to drop off from this study at any time without penalty or loss of your current benefits.

BENEFITS OF THE STUDY

Direct benefits include receiving oral health information and counseling. You will also receive free sugar-free drink samples. You and your child may or may not experience a direct health benefit. However, by switching from sugared-fruit drinks to sugar-free fruit drinks, we expect your child to have less sugar intake and fewer cavities.

SOURCE OF FUNDING

The study is funded by the National Institutes of Health.

CONFIDENTIALITY OF RESEARCH INFORMATION

Information about this study will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that identify you. You can search this Web site at any time.

You and your children's information are confidential. The samples and information you and your child provide will be stored with only an identification number. Your and your child's name will not appear on the samples and information. Only de-identified information and samples will be provided to the researcher doing the analysis. Your name on the consent form will be kept separate from the information you provide for the study. Identifying information will be stored in locked file cabinets at the University of Washington.

We submit research findings to the YKHC Board for review and approval before we make them public in professional journals, other news media, or presentations. When research findings are reported in a professional setting, such as in a medical journal or at a scientific meeting, we will not identify you and your community.

We have a Certificate of Confidentiality from the federal National Institutes of Health. This helps us protect your privacy. The Certificate means that we do not have to give out identifying

information about you even if we are asked to by a court of law. We will use the Certificate to resist any requests for identifying information.

We can't use the Certificate to withhold your research information if you give your written consent to give it to an insurer, employer, or other person. Also, you or a member of your family can share information about yourself or your part in this research if you wish.

There are some limits to this protection. We will voluntarily provide the information to:

- a member of the federal government who needs it in order to audit or evaluate the research;
- individuals at the University of Washington, the funding agency, and other groups involved in the research, if they need the information to make sure the research is being done correctly;
- the FDA, if required by the FDA;
- state or local authorities, if we learn of child abuse, elder abuse, or the intent to harm yourself or others.

Government or university staff sometimes review studies to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

USE OF INFORMATION AND SPECIMENS

The information you provide in this study may be used for future research studies related to oral health. It is also possible that in the future we may want to use or share study information that might identify you. If we do, we will obtain additional consent from you at that time.
You and your child's hair and oral plaque samples belong to you. These samples will be stored at UW and UAF. All the samples are stored with only an identification number. Your and your child's name will not appear on your samples. Analyses of your hair samples will be conducted under the direction of Dr. Diane O'Brien, a collaborator on this project. Plaque samples will be stored at UW in a secure freezer for analysis at a later date. This research does not involve giving treatment or other medical care as a part of the study. It only involves using this information to better understand sugar intake and cavities among Alaska Native children. You and your child's hair samples will be destroyed after analysis; there will not be any remaining unused samples. The information that we obtain from you and your child's hair and plaque samples will not have any identifying information.

We would like to store your child's plaque samples for future analyses. We want to know if the program changed the types of bacteria in your child's mouth. The reason we are storing the samples is that we currently do not have funding to analyze the plaque samples. Regardless of future analyses, all plaque specimens will be destroyed by 2027. If you don't want your child's plaque samples stored, they can still be in the study. It will not change their participation. You may ask to have your child's samples removed from our freezers at any time. Call Dr. Donald Chi, at 206-616-4332.

☐ I agree to have my child's plaque samples stored for future analyses.

Participant Initials:_____

☐ I DO NOT agree to have my child's plaque samples stored for future analyses.

RESEARCH-RELATED INJURY

If you think you have been harmed from being in this research, contact Dr. Donald Chi at 1-206-616-4332 or e-mail him at dchi@uw.edu or Dr. Joseph Klejka, YKHC Vice President of Quality, in Bethel at (907) 543-6028.

Printed name of study staff obtaining consent Signature Date

Participant's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research participant, I can call the University of Washington Human Subjects Division at (206) 543-0098 or call collect at (206) 221-5940. I will receive a copy of this consent form.

Printed name of participant Signature of participant Date

Home address Phone number

Printed name of Yup'ik translator Signature of translator Date

Copies to: Researcher | Participant

APPENDIX M: ADULT CONSENT FORM (CONTROL – MODIFIED INTERVENTION)

Study Participation Consent & Parental Permission Form: Control Arm – Modified Intervention

Reducing Sugared Fruit Drinks in Alaska Native Children

Main Researchers: Dr. Donald Chi, Professor, University of Washington, School of Dentistry, Department of Oral Health Sciences, 206-616-4332

Researchers' Statement

We are asking you and your child to be in a research study. The purpose of this consent form is to give you the information you'll need to help you decide if you want to be in the study or not. Please read the form carefully. You may ask any questions about the research or this form. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called "informed consent." We will give you a copy of this form for your records.

PURPOSE OF THE STUDY

The study goal is to learn if a community program can help Yup'ik children to drink less sugary drinks and have fewer cavities. Your community was originally assigned to the control community. Now you will have the opportunity to receive a modified version of the intervention based on information we gathered from the first part of the study.

STUDY PROCEDURES

The study will last about 6 months. We will ask you and your child to join us at the Community Clinic 2 more times after today. A trained staff person will ask you questions about your children's diet, measure your child's weight, use scissors to cut about 20 strands of hair from yourself and your child and collect an oral plaque specimen using a swab. Each visit will last up to 1 and 1/2 hours. You will receive a $50 store gift card per child after completing each visit. At each visit, we will ask for your feedback about the health program. We would like to audio record the conversations if that is okay with you. You can review transcripts of the conversations if you would like.

In addition, a trained Community Health Worker (CHW) or University of Washington study staff member will contact you and your child 6 times during the 6-month study period. Each visit will last 5 to 30 minutes. The visits may be in person, virtual, or by phone. In the first visit, we will show information about fruit drinks and cavities. In the second visit, we will introduce you to sugar-free drinks. During the third and fourth visits, we will work with you to improve ways to get your child to accept healthier drinks. After that, there will be two brief-check-in visits to see your progress in the program. In case there is a COVID-19 risk we will use a mask and other precautions such as social distancing.

RISKS, STRESS, OR DISCOMFORT

You may feel uncomfortable participating in our study in some situations. First, in some cases, when children have too many sugar-free fruit drinks, they might have an upset tummy or runny stool. These side effects may also occur in adults. Sugar-free fruit drinks are FDA-approved and

safe for children when they drink the right amount. To be safe, families who participate in our program should follow the mixing instructions. Caregivers need to keep an eye on the number of sugar-free drinks they and their child have.

Second, there is a chance that other community members may be aware of your participation in our study. That may make you feel uncomfortable. However, your personal information will be securely stored. We will not share your information with anyone besides our study staff.

Third, you and your children may feel uncomfortable about providing your weight, hair and oral plaque samples. You may also feel uncomfortable sharing what your children ate. If you or your children feel any discomfort, you may stop participating at any time. Your decision will not change the care that you and your child receive from YKHC. You and your child may say no to any part of the study. You and your child are free to drop off from this study at any time without penalty or loss of your current benefits.

BENEFITS OF THE STUDY

Direct benefits include receiving oral health information and counseling. You will also receive free sugar-free drink samples. You and your child may or may not experience a direct health benefit. However, by switching sugared-fruit drinks to sugar-free fruit drinks, we expect your child to have less sugar intake and cavities.

SOURCE OF FUNDING

The study is funded by the National Institutes of Health.

CONFIDENTIALITY OF RESEARCH INFORMATION

Information about this study will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. You can search this Web site at any time.

You and your children's information are confidential. The samples and information you and your child provide will be stored with only an identification number. Your and your child's name will not appear on the samples and information. Only de-identified information and samples will be provided to the researcher doing the analysis. Your name on the consent form will be kept separate from the information you provide for the study. Identifying information will be stored in locked file cabinets at the University of Washington.

We submit research findings to the YKHC Board for review and approval before we make them public in professional journals, other news media, or presentations. When research findings are reported in a professional setting, such as in a medical journal or at a scientific meeting, we will not identify you and your community.

We have a Certificate of Confidentiality from the federal National Institutes of Health. This helps us protect your privacy. The Certificate means that we do not have to give out identifying information about you even if we are asked to by a court of law. We will use the Certificate to resist any requests for identifying information.

We can't use the Certificate to withhold your research information if you give your written consent to give it to an insurer, employer, or other person. Also, you or a member of your family can share information about yourself or your part in this research if you wish.

There are some limits to this protection. We will voluntarily provide the information to:

- a member of the federal government who needs it in order to audit or evaluate the research;
- individuals at the University of Washington, the funding agency, and other groups involved in the research, if they need the information to make sure the research is being done correctly;
- the FDA, if required by the FDA;
- state or local authorities, if we learn of child abuse, elder abuse, or the intent to harm yourself or others.

The Certificate expires when the NIH funding for this study ends. Currently this is March 31, 2023. Any data collected after expiration is not protected, as described above. Data collected prior to expiration will continue to be protected.

Government or university staff sometimes review studies to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

USE OF INFORMATION AND SPECIMENS

The information you provide in this study may be used for future research studies related to oral health. It is also possible that in the future we may want to use or share study information that might identify you. If we do, we will obtain additional consent from you at that time.
You and your child's hair and oral plaque samples belong to you. These samples will be stored at UW and UAF. All the samples are stored with only an identification number. Your and your child's name will not appear on your samples. Analyses of your hair samples will be conducted under the direction of Dr. Diane O'Brien, our collaborator on this project. Plaque samples will be stored at UW in a secure freezer for analysis at a later date. This research does not involve giving treatment or other medical care as a part of the study. It only involves using this information to better understand sugar intake and cavities among Alaska Native children. You and your child's hair samples will be destroyed after analysis; there will not be any remaining unused sample. The information that we obtain from you and your child's hair and plaque samples will not have any identifying information.

We would like to store your child's plaque samples for future analyses. We want to know if the program changed the types of bacteria in your child's mouth. The reason we are storing the samples is that we currently do not have funding to analyze the plaque samples. Regardless of future analyses, all plaque specimens collected will be destroyed by 2029. If you don't want your child's plaque samples stored, they can still be in the study. It will not change their participation. You may

ask to have your child's samples removed from our freezers at any time. Call Dr. Donald Chi, at 206-616-4332.

☐ I agree to have my child's plaque samples stored for future analyses.

Participant Initials:_____

☐ I DO NOT agree to have my child's plaque samples stored for future analyses.

RESEARCH-RELATED INJURY

If you think you have been harmed from being in this research, contact Dr. Donald Chi at 1-206-616-4332 or e-mail him at dchi@uw.edu or Dr. Joseph Klejka, YKHC Vice President of Quality, in Bethel at (907) 543-6028.

Printed name of study staff obtaining consent Signature Date

Participant's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research participant, I can call the University of Washington Human Subjects Division at (206) 543-0098 or call collect at (206) 221-5940. I will receive a copy of this consent form.

Printed name of participant Signature of participant Date

_____

Home address Phone number

_____

Printed name of Yup'ik translator Signature of translator Date

Copies to: Researcher | Participant

APPENDIX N: ASSENT FORM (INTERVENTION)

Study Participation Assent to Research Form: Intervention Arm

Reducing Sugared Fruit Drinks in Alaska Native Children

Main Researchers: Dr. Donald Chi, Professor, University of Washington, School of Dentistry, Department of Oral Health Sciences, 206-616-4332

Researcher's statement:

My name is [*identify yourself to the child by name*].

We are asking you to be in a research study. We are trying to introduce a health program to help you switch from juices like Tang and Kool-Aid to sugar-free Tang and Kool-Aid.

If you agree to be in this study, we will have 9 visits with you over the next 6 months. We will ask you to watch a video about juice and cavities. We will ask you to pick your favorite flavors and help make and taste sugar-free juices with your family.

Then we will ask you and your caregiver to come to the clinic 5 times so we can ask you questions about foods you have eaten and what you have had to drink in the past 24 hours. We will also weigh you, ask for a small sample of hair, and take a dental plaque sample (white sticky staff from your teeth that can scratch off) from your mouth.

The benefits of the program include getting oral health information and samples of the sugar-free juice. If you don't want to be in the study, you don't have to participate. Remember, being in this study is up to you, and no one will be upset if you don't want to participate or even if you change your mind later and want to stop. You can ask any questions about the study. If you have a question later, you can call me [*insert telephone number*] or ask me next time.

Please talk this over with your parents before you decide whether or not to do this. We will also ask your parents if it is okay for you to be in this study. Even if your parents say "yes," you can still decide not to do this.

Printed name of study staff obtaining consent	Signature	Date

Your statement:
This research has been explained to me. I agree to take part in this study. I have had a chance to ask questions. If I have more questions, I can ask the researcher.
Writing your name at the bottom means that you agree to be in this study. You and your parents will be given a copy of this form after you have signed it.

Printed name of participant Date

Copies to:
Participant
Researcher's file

APPENDIX O: ASSENT FORM (CONTROL)

Study Participation Assent to Research Form: Control Arm

Reducing Sugared Fruit Drinks in Alaska Native Children

Main Researcher: Dr. Donald Chi, Associate Professor, University of Washington, School of Dentistry, Department of Oral Health Sciences, 206-616-4332

Researcher's statement:
My name is [*identify yourself to the child by name*].

We are asking you to be in a research study. We are trying to see if a health program can help Yup'ik children to switch from juices like Tang and Kool-Aid to sugar-free Tang and Kool-Aid.

If you agree to be in this study, we will ask you and your caregiver to come to the clinic 5 times so we can ask you questions about foods you have eaten and what you have had to drink in the past 24 hours. We will also weigh you, ask for a small sample of hair, and take a dental plaque sample (white sticky stuff from your teeth that can scratch off) from your mouth.

Then we will visit with you 9 times, if you like us to. We will ask you to watch a video about juice and cavities. We will ask you to pick your favorite flavors and help make and taste sugar-free juices with your family.

The benefits of the program include getting oral health information and samples of the sugar-free juice. If you don't want to be in the study, you don't have to participate. Remember, being in this study is up to you, and no one will be upset if you don't want to participate or even if you change your mind later and want to stop. You can ask any questions about the study. If you have a question later, you can call me [*insert your telephone number*] or ask me next time.

Please talk this over with your parents before you decide whether or not to do this. We will also ask your parents if it is okay for you to be in this study. Even if your parents say "yes," you can still decide not to do this.

Printed name of study staff obtaining consent	Signature	Date

Your statement:
This research has been explained to me. I agree to take part in this study. I have had a chance to ask questions. If I have more questions, I can ask the researcher.
Writing your name at the bottom means that you agree to be in this study. You and your parents will be given a copy of this form after you have signed it.

Printed name of participant Date

Copies to:
Participant
Researcher's file

APPENDIX P: ASSENT FORM (CONTROL – MODIFIED INTERVENTION)

Study Participation Assent to Research Form: Control Arm – Modified Intervention

Reducing Sugared Fruit Drinks in Alaska Native Children

Main Researchers: Dr. Donald Chi, Professor, University of Washington, School of Dentistry, Department of Oral Health Sciences, 206-616-4332

Researcher's statement:

My name is [*identify yourself to the child by name*].

We are asking you to be in a research study. We are trying to introduce a health program to help you switch from juices like Tang and Kool-Aid to sugar-free Tang and Kool-Aid.

If you agree to be in this study, we will have 5-9 visits with you over the next 6 months. We will ask you to watch a video about juice and cavities. We will ask you to pick your favorite flavors and help make and taste sugar-free juices with your family.

Then we will ask you and your caregiver to come to the clinic 2 times so we can ask you questions about foods you have eaten and what you have had to drink. We will also weigh you, ask for a small sample of hair, and take a dental plaque sample (white sticky staff from your teeth that can scratch off) from your mouth.

The benefits of the program include getting oral health information and samples of the sugar-free juice. If you don't want to be in the study, you don't have to participate. Remember, being in this study is up to you, and no one will be upset if you don't want to participate or even if you change your mind later and want to stop. You can ask any questions about the study. If you have a question later, you can call me [*insert telephone number*] or ask me next time.

Please talk this over with your parents before you decide whether or not to do this. We will also ask your parents if it is okay for you to be in this study. Even if your parents say "yes," you can still decide not to do this.

Printed name of study staff obtaining consent Signature Date

Your statement:
This research has been explained to me. I agree to take part in this study. I have had a chance to ask questions. If I have more questions, I can ask the researcher.
Writing your name at the bottom means that you agree to be in this study. You and your parents will be given a copy of this form after you have signed it.

Printed name of participant Date

Copies to:
Participant
Researcher's file

APPENDIX Q: POST-INTERVENTION INTERVIEW GUIDE (6-month)

An Intervention to Reduce Sugared Fruit Drinks in AK Native Children
Semi-Structure Interview Script
6m data collection visit

1. How is everything going with the sugar-free Kool Aid? Good, okay, not good, other (_____)
    a. Tell me more (what's going good, what's not good, why just ok)

2. Do your children like the sugar-free Kool Aid? Yes, no, other (_____)
    a. Is it the same for all your children? If different for children, tell me more.
    b. How about the adults in your family? Do they like them?

3. Have you experienced any difficulties getting your children to drink the sugar-free Kool Aid at home? Yes, No, other (_____)
    a. If yes, tell me more about barriers encountered.
    b. Have the Community Health Workers been able to help problem solve?

4. Have you used your vouchers at the local store? Yes, no, other (_____)
    a. Tell me more about any difficulties in redeeming the vouchers

5. Have you been able to purchase additional sugar-free Kool Aid drops at the local store? Yes, no, other (_____)
    a. Tell me more about your ability to purchase more at your local store

6. Are there times when you give your children regular sugared Kool Aid? Yes, no, other (_____)
    a. Tell me more (when, reason why).

7. Will you continue giving your children the sugar-free Kool Aid? Yes, no, other (_____)
    a. Tell me more (if yes, why? If no, why?)
    b. Is there anything that could make this easier for you?

8. Has the program changed what your child drinks at home? Yes, no, other (_____)
    a. Tell me more (less sugared Kool Aid, same as before the program)

9. What's been your overall experience with our program? Good, okay, not good
    a. Tell me more.

10. Is there anything about the program you would change? Yes, no, other (_____)
    a. Tell me more (what would you change, what would you keep the same)

APPENDIX R: POST ST-INTERVENTION INTERVIEW GUIDE [INTERVENTION] (12-month)

An Intervention to Reduce Sugared Fruit Drinks in AK Native Children
Semi-Structure Interview Script
12M data collection visit [INTERVENTION]

[Sugar-free Kool-Aid refers to the drops we provided as part of the program]

1. **Will you continue giving your children the sugar-free Kool Aid drops?** (YES, NO, OTHER) [Check their response on their answer sheet]

    a. If ***YES***:
        i. Tell me more about why.
        ii. What would it easier for you to continue?
        iii. What would make it difficult to continue?

    b. If ***NO***:
        i. Why not?

2. **Have you purchased additional sugar-free Kool Aid drops at the local store?** (YES, NO, OTHER) [Check their response on their answer sheet]

    a. If ***YES***:
        i. About how many times did you buy them?
        ii. Were they easy to find?
        iii. What do you think about the price?
        iv. Do you plan on buying more in the future?

    b. If ***NO***:
        i. Why not?
        ii. Have you purchased them somewhere else?

3. **Has the program changed what your children drink at home?** (YES, NO, OTHER)
    a. In what ways has the program changed what your children drink at home?
    If more than one child in the home: Is this the same for all your children?

4. **What's been your overall experience with our program?** (GOOD, BAD, OTHER)
    a. Tell me more about why you said *[GOOD, BAD, OTHER]*

5. Another part of the program involved collecting data from you and your child/children. **Tell me about your experiences with the data collection part of the study.** (GOOD, BAD, OTHER).
    a. Tell me more (i.e., specific procedures (hair and plaque collection), time)

6. **Is there anything about the program you would change?** (YES, NO, OTHER)
    a. Tell me what you would change (and what you would keep the same).
    b. How long does it take for your visits? (Tell me more…)
    c. How can we make the program visits easier and pleasant? (Tell me more…)

7. **Would you recommend that other communities start this program?** (YES, NO, OTHER)
    a. Why or why not?

APPENDIX S: POST-INTERVENTION INTERVIEW GUIDE [CONTROL] (12-month)

An Intervention to Reduce Sugared Fruit Drinks in AK Native Children
Semi-Structure Interview Script
12m data collection visit [CONTROL]

[Sugar-free Kool-Aid refers to the drops we provided as part of the program]

1. Part of the program involved collecting data from you and your child/children.
   Tell me about your experiences with the data collection part of the study.
   (GOOD, BAD, OTHER).
   a. Tell me more (i.e., specific procedures (hair and plaque collection), time)

2. **Is there anything about the program you would change?**
   (YES, NO, OTHER)
   a. Tell me what you would change (and what you would keep the same).
   b. How long does it take for your visits? (Tell me more…)
   c. How can we make the program visits easier and pleasant? (Tell me more…)

APPENDIX T: POST-INTERVENTION INT. CATEGORIAL QUESTIONS FOR PARTICIPANT (12-month)

REDUCING SUGARED FRUIT DRINKS IN ALASKA NATIVE CHILDREN
INTERVENTION INTERVIEW
12M VISIT – SEPTEMBER 2023

This section is to be completed by UW Study staff.

DATE:_____/_____/_____ TIME:_____ COMMUNITY: _____

Household ID:_____ Caregiver ID:_____

Please answer the questions on this form.

[Sugar-free Kool-Aid refers to the drops we provided as part of the program]

For each of the following, please circle one response.			
Are your children drinking the sugar-free Kool-Aid drops?	Yes	No	Other
Do they drink-	Sugar-free only	Combination of sugar-free and sugared	Only sugared drink
Would you say all of your children like the sugar-free Kool-Aid drops	A lot	A little	Not at all
Have you experienced any difficulties getting your children to drink the sugar-free Kool Aid drops at home?	Yes	No	Other
Did your children like the sugar-free Kool-Aid drops when we first introduced them?	Yes	No	Other
How about the adults in your family - Do they like them? Do them drink them?	Yes	No	Other
Will you continue giving your children the sugar-free Kool Aid drops?	Yes	No	Other
Have you purchased additional sugar-free Kool Aid drops at the local store?	Yes	No	Other
Have you purchased additional sugar-free Kool Aid drops online?	Yes	No	Other

Quyana for your responses!

REDUCING SUGARED FRUIT DRINKS IN ALASKA NATIVE CHILDREN
INTERVENTION INTERVIEW
12M VISIT – SEPTEMBER 2023

As part of our program, we showed you videos, practiced how to mix the sugar-free Kool-Aid, provided you with samples, gave you vouchers to use at the local store, and you met with the CHW several times. *For each of the following, please circle one response.*			
Has the program changed what your children drink at home?	**Yes**	**No**	**Other**
What's been your overall experience with our program?	**Good**	**Bad**	**Other**

For each part of the program, we would like your thoughts on how helpful or unhelpful each part was in getting your child/children to drink sugar-free Kool-Aid. *For each of the following, please circle one response.*			
Showing you the videos.	**Helpful**	**Not Helpful**	**Other**
Practicing how to mix the sugar-free Kool-Aid.	**Helpful**	**Not Helpful**	**Other**
Providing you with samples to take home.	**Helpful**	**Not Helpful**	**Other**
Giving you vouchers to use at the local store.	**Helpful**	**Not Helpful**	**Other**

APPENDIX U: BEVERAGE QUESTIONNAIRE

You will be asked about ***HOW OFTEN*** & ***HOW MUCH*** of each type of beverage your child drinks in the past month.

Types of Beverages							
Water	**Sugar-Free Kool-Aid** (concentrated juice bottles)	**Sweetened Juice** (regular Kool-Aid, Tang, lemonade)	**100% Fruit Juice**	**Soda Pop** or **Soft Drinks** (coke, sweet tea)	**Diet Soda Pop** or **Artificially Sweetened Soft Drinks** (diet coke, crystal light)	**Sports Drinks** or **Energy Drinks** (Gatorade, monster)	**Milk**
							

How *OFTEN* ?						
Never or less than once per *week*	**Once** per *week*	**2-3 times** per *week*	**4-6 times** per *week*	**1 or more times** per *day*	**2 or more times** per *day*	**3 or more times** per *day*

How *MUCH* ?				
Less than 6oz (3/4 cup)	**8oz (1 cup)**	**12oz (1 ½ cups)**	**16oz (2 cups)**	**More than 20oz (2 ½ cups)**

Beverage Questionnaire

READ TO THE PARTICIPANT: **"In the past MONTH (for each child), I will ask you to indicate 'how often' and 'how much' of each beverage your child drank.**

Show the BEVQ hard copy to the particpiant when asking questions and collecting responses.

***Do NOT count beverages used in cooking or other preparations, such as milk in cereal**

For example: Ask "In the past month, how often did [CHILDXXXX] drink water?"

Record the apropriate response in the survey item for water below.

Then ask "How much water did [CHILDXXXX] drink each time?"

Record the apropriate response in the survey item for water below.

Enter the child PID for the "first child"	3001
Are you the person who prepares ***most*** of the meals for this child?	Yes
In the past month, ***how often*** did 3001 drink **WATER**?	○ never or < 1 per week ○ 1 time per week ◉ 2-3 times per week ○ 4-6 times per week ○ 1 time per day ○ 2+ times per day ○ 3+ times per day reset
How much **WATER** did 3001 drink each time?	○ < 6 fl oz (3/4 cup) ○ 8 fl oz (1 cup) ○ 12 fl oz (1 1/2 cups) ○ 16 fl oz (2 cups) ○ More than 20 fl oz (2 1/2 cups) reset
In the past month, ***how often*** did 3001 drink **SUGAR-FREE KOOL-AID** (from the concentrated 'juice' bottles)?	◉ never or < 1 per week ○ 1 time per week ○ 2-3 times per week ○ 4-6 times per week ○ 1 time per day ○ 2+ times per day ○ 3+ times per day reset
In the past month, ***how often*** did 3001 drink **SWEETENED JUICE** (e.g., KOOL-AID, TANG, LEMONADE, SUNNY DELIGHT)?	○ never or < 1 per week ○ 1 time per week ○ 2-3 times per week ○ 4-6 times per week ◉ 1 time per day ○ 2+ times per day ○ 3+ times per day reset
How much SWEETENED JUICE did 3001 drink each time?	○ < 6 fl oz (3/4 cup) ○ 8 fl oz (1 cup) ○ 12 fl oz (1 1/2 cups) ○ 16 fl oz (2 cups) ○ More than 20 fl oz (2 1/2 cups) reset

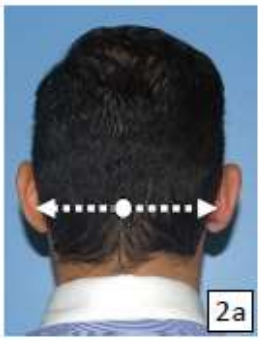
In the past month, ***how often*** did 3001 drink **100% FRUIT JUICE**?	○ never or < 1 per week ○ 1 time per week ◉ 2-3 times per week ○ 4-6 times per week ○ 1 time per day ○ 2+ times per day ○ 3+ times per day reset
***How much* 100% FRUIT JUICE** did 3002 drink each time?	○ < 6 fl oz (3/4 cup) ○ 8 fl oz (1 cup) ○ 12 fl oz (1 1/2 cups) ○ 16 fl oz (2 cups) ○ More than 20 fl oz (2 1/2 cups) reset
In the past month, ***how often*** did 3002 drink **SWEETENED JUICE** (e.g., KOOL-AID, TANG, LEMONADE, SUNNY DELIGHT)?	○ never or < 1 per week ○ 1 time per week ○ 2-3 times per week ○ 4-6 times per week ◉ 1 time per day ○ 2+ times per day ○ 3+ times per day reset
How much SWEETENED JUICE did 3002 drink each time?	○ < 6 fl oz (3/4 cup) ○ 8 fl oz (1 cup) ○ 12 fl oz (1 1/2 cups) ○ 16 fl oz (2 cups) ○ More than 20 fl oz (2 1/2 cups) reset
In the past month, ***how often*** did 3002 drink **SODA POP or SOFT DRINKS** (e.g., coke, sweet tea)	○ never or < 1 per week ◉ 1 time per week ○ 2-3 times per week ○ 4-6 times per week ○ 1 time per day ○ 2+ times per day ○ 3+ times per day reset
How much SODA POP or SOFT DRINKS *(e.g., coke, sweet tea)* did 3002 drink each time?	○ < 6 fl oz (3/4 cup) ○ 8 fl oz (1 cup) ○ 12 fl oz (1 1/2 cups) ○ 16 fl oz (2 cups) ○ More than 20 fl oz (2 1/2 cups) reset
In the past month, ***how often*** did 3002 drink **DIET SODA POP or ARTIFICIALLY SWEETNED SOFT DRINKS NOT including the sugar-free kool aid** (e.g., diet coke, crystal light)?	◉ never or < 1 per week ○ 1 time per week ○ 2-3 times per week ○ 4-6 times per week ○ 1 time per day ○ 2+ times per day ○ 3+ times per day reset
In the past month, ***how often*** did 3002 drink **SPORTS DRINKS or ENERGY DRINKS** (e.g., gatorade, monster)?	◉ never or < 1 per week ○ 1 time per week ○ 2-3 times per week ○ 4-6 times per week ○ 1 time per day ○ 2+ times per day ○ 3+ times per day reset

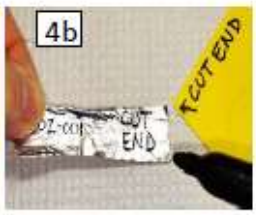
In the past month, ***how often*** did 3001 drink **MILK**?	○ never or < 1 per week ○ 1 time per week ○ 2-3 times per week ○ 4-6 times per week ◉ 1 time per day ○ 2+ times per day ○ 3+ times per day reset
What kind of **MILK** was this?	○ Whole Milk ○ Reduced Fat Milk (2%) ○ Low Fat/Fat Free Milk (Skim, 1%, Buttermilk, Soy or Nut Alternative) reset
How much MILK did 3001 drink each time?	○ < 6 fl oz (3/4 cup) ○ 8 fl oz (1 cup) ○ 12 fl oz (1 1/2 cups) ○ 16 fl oz (2 cups) ○ More than 20 fl oz (2 1/2 cups) reset

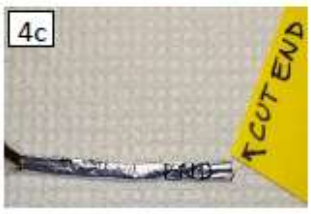
APPENDIX V: INSTRUCTIONS FOR COLLECTION OF HAIR SAMPLES

O'Brien Lab at UAF | 907.474.5762 | May 2020

Hair Collection Method - Hair Longer Than 1 Inch







1. Don a mask and use hand sanitizer to clean hands. Clean scissors between participants. Maintain social distancing except when collecting the sample.
2. Take a pinch of hair from <u>below</u> the bump at the back of the head, where the ○ is in the pictures (1a and 2a). If the hair is long, part it (1a). The pinch should be about this thick ● . If the hair is long, twist the hair (1b).
3. Cut the hair close to the skin (1c and 2b). Picture 3 shows the cut end. Be careful to keep the hairs lined up at the cut end.
4. Put the hair in the foil and fold the foil lengthwise twice (4a and 4b). It is OK if the non-cut end sticks out of the foil.
5. Write 'CUT END' on the end of the foil where the cut end of the hair is (4b). Write the sample number on the other end. Fold again (4c).
6. Put the wrapped hair in the bag. Write the sample number on the bag (4d).

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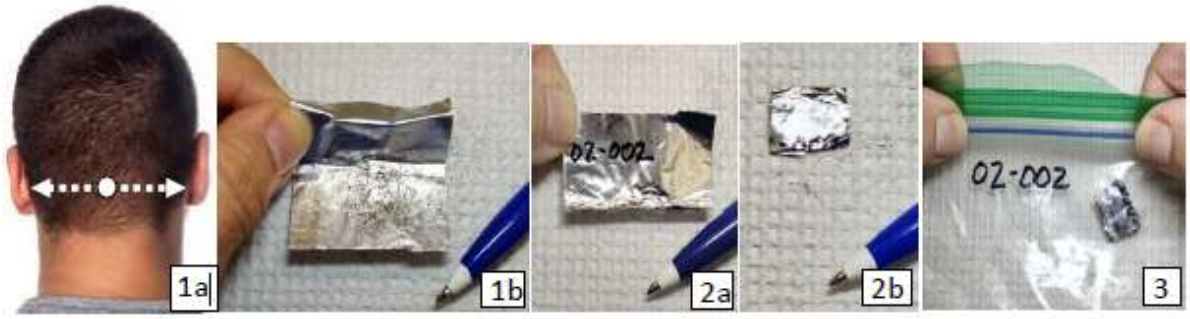
Hair Collection Method - SHAVED HEADS



1. Don a mask and use hand sanitizer to clean hands. Clean scissors between participants. Maintain social distancing except when collecting the sample.
2. Cut a small patch of hair of about this thick ● into the foil from below the bump at the back of the head, where the ○ is in the picture (1a and 1b).
3. Fold the foil closed and write the sample number on the foil (2a).
4. Fold it two more times (2b).
5. Put the folded foil in bag.
6. Write the sample number on the bag (3).