# Birth to Three – Cavity Free: Effectiveness of a Psychoeducational Intervention for ECC Prevention

**Unique Protocol Identification Number: UH3DE029443**
**National Clinical Trial (NCT) Identified Number: 05756413**
**Principal Investigator: Karin Weber-Gasparoni**
**Sponsor: University of Iowa**

**Grant Title: Birth to Three – Cavity Free: Effectiveness of a Psychoeducational Intervention for ECC Prevention**
**Grant Number: 22-031-E**
**Version Number: 0.7**
**July 2, 2024**

## Summary of Changes from Previous Version:

| Version Number | Date | Affected Section(s) | Summary of Revisions Made | Rationale |
|---|---|---|---|---|
| 0.1 | 08/04/21 | Comments through Section 7 | Melissa Riddle added comments to this draft, as the first NIDCR review of the protocol | Comments are suggestions to consider, largely meant to follow the language and level of detail that is familiar to the NIDCR clinical team; let's discuss any comments that don't make sense or seem misguided |
| 0.2 | 03/04/22 | Changes made on 4.1 Overall Design section | Melissa Riddle and Elise Rice reviewed transition package with PI and CTRA during zoom meeting | Clarification regarding the recruitment window of potential pregnant women |
| 0.3 | 4/27/22 | Changes made on the following sections: Table of Contents; 5.2 Exclusion Criteria; 5.4 Screen Failures; | University of Iowa IRB requested to remove exclusion criteria | 1) Mothers who deliver their child prior to their first study intervention visit – according to IRB, mothers no longer meet the inclusion |

| | | | | |
|---|---|---|---|---|
| | | 6.2.1 Interventionist Training and Tracking (e.g., Research Team Staff and WIC Clinic Staff) | | criteria of being pregnant to participate in the study.<br>2) Children born with medical and/or special health care needs conditions that require specialized care and/or hospitalization preventing the mother to participate in study activities – according to IRB, this is the mother's choice to withdraw from the study. |
| 0.4 | 6/21/22 | Changes made on section 7.2 Participant Discontinuation/Withdrawal from the Study | Elise Rice in email dated 6/20/22 requested a revision on section 7.2 to specify mother's choice to withdraw from study if their child is born with medical and/or special health care needs conditions | NIH team suggested the update on section 7.2 to match IRB request to change the exclusion criteria above to a participant discontinuation/withdrawal |
| 0. 5 | 8/16/22 | Several sections | Several revisions made | Revisions made suggested by RHO |
| | | | | |
| 0.6 | 1/29/24 | Sections 4.3 and 6.1.2 | Clarified criteria for optional nature of the Year 1 Month 3 booster videos | Revisions made suggested by RHO |
| 0.7 | 2/9/24 | Sections 4.1, 5.1, 5.5, Table of Detailed Description of Study Procedures, Sections 5.5. and 6.4, 10.1.5 updated Key Roles and Governance table | Updated gestational window for recruiting moms from 32-36 wks, can start interventions earlier at 16 wks vs. 24.<br>Updated widening of 1- and 9-month questionnaires to eight weeks.<br>Updates of research team members, recruitment sites | DSMB recommendations from 11/29/24 meeting<br><br>General updates to study |

| | | | | |
|---|---|---|---|---|
| 0.7 | 7/14/24 | Section 6.1.2 | Change language to reflect that "Visit 2, 3 and 4 will be scheduled based upon the child's DOB and will take place when the child is approximately 12, 24 and 36 months of age." | Revisions made suggested by RHO |
| | | | Added language to reflect that according to informed consent approved by the UI IRB, "You (study participant) may feel uncomfortable in answering certain questions and you can choose to decline any aspect of the study at any time. You and your child may discontinue participating at any time without any negative consequences." Therefore, participants may choose not to complete the one-month follow-up questionnaires," which means that a protocol deviation does not occur when mothers do not complete the 1- and 9-month follow-up questionnaires. | Revision to address RHO Action Items #s 21 and 22 dated 2024-7-11_12 |

## Table of Contents

Statement of Compliance....6
Investigator's Signature....6
1 Protocol Summary....7
1.1 Synopsis....7
1.2 Schema....9
1.3 Schedule of Activities....10
2 Introduction....11
2.1 Study Rationale....11
2.2 Background....12

2.3 Risk/Benefit Assessment ..... 15
2.3.1 Known Potential Risks ..... 15
2.3.2 Known Potential Benefits ..... 16
2.3.3 Assessment of Potential Risks and Benefits ..... 16
3 Objectives and Endpoints ..... 17
4 Study Design ..... 23
4.1 Overall Design ..... 23
4.2 Scientific Rationale for Study Design ..... 23
4.3 Justification for Intervention ..... 24
4.4 End-of-Study Definition ..... 24
5 Study Population ..... 25
5.1 Inclusion Criteria ..... 25
5.2 Exclusion Criteria ..... 25
5.3 Lifestyle Considerations ..... 25
5.4 Screen Failures ..... 25
5.5 Strategies for Recruitment and Retention ..... 25
6 Study Intervention(s) or Experimental Manipulation(s) ..... 28
6.1 Study Intervention(s) or Experimental Manipulation(s) Administration ..... 28
6.1.1 Study Intervention or Experimental Manipulation Description ..... 28
6.1.2 Administration and/or Dosing ..... 28
**Detailed Description of the Study Intervention** ..... 30
**Detailed Description of the Study Procedures** ..... 31
6.2 Fidelity ..... 31
6.2.1 INTERVENTIONIST TRAINING AND TRACKING ..... 31
6.3 Measures to Minimize Bias: Randomization and Blinding ..... 32
6.4 Study Intervention/Experimental Manipulation Adherence ..... 32
6.5 Concomitant Therapy ..... 33
6.5.1 Rescue Procedures ..... 33
7 Study Intervention/Experimental Manipulation Discontinuation and Participant Discontinuation/Withdrawal ..... 34
7.1 Discontinuation of Study Intervention/Experimental Manipulation ..... 34
7.2 Participant Discontinuation/Withdrawal from the Study ..... 34
7.3 Lost to Follow-Up ..... 34
8 Study Assessments and Procedures ..... 36
8.1 Endpoint and Other Non-Safety Assessments ..... 36
8.2 Safety Assessments ..... 37
8.3 Adverse Events and Serious Adverse Events ..... 37
8.3.1 Definition of Adverse Events ..... 37
8.3.2 Definition of Serious Adverse Events ..... 37
8.3.3 Classification of an Adverse Event ..... 38
8.3.4 Time Period and Frequency for Event Assessment and Follow-Up ..... 38
8.3.5 Adverse Event Reporting ..... 39
8.3.6 Serious Adverse Event Reporting ..... 39
8.3.7 Reporting Events to Participants ..... 40
8.3.8 Events of Special Interest ..... 40
8.3.9 Reporting of Pregnancy ..... 40
NA ..... 40
8.4 Unanticipated Problems ..... 40
8.4.1 Definition of Unanticipated Problems ..... 40
8.4.2 Unanticipated Problems Reporting ..... 40

8.4.3 Reporting Unanticipated Problems to Participants ..... 41
9 Statistical Considerations ..... 42
9.1 Statistical Hypotheses ..... 42
9.2 Sample Size Determination ..... 42
9.3 Populations for Analyses ..... 43
9.4 Statistical Analyses ..... 43
9.4.1 General Approach ..... 43
9.4.2 Analysis of the Primary Endpoint(s) ..... 43
9.4.3 Analysis of the Secondary Endpoint(s) ..... 44
9.4.4 Safety Analyses ..... 45
9.4.5 Baseline Descriptive Statistics ..... 45
9.4.6 Planned Interim Analyses ..... 45
9.4.7 Sub-Group Analyses ..... 45
9.4.8 Tabulation of Individual Participant Data ..... 45
9.4.9 Exploratory Analyses ..... 45
10 Supporting Documentation and Operational Considerations ..... 46
10.1 Regulatory, Ethical, and Study Oversight Considerations ..... 46
10.1.1 Informed Consent Process ..... 46
10.1.2 Study Discontinuation and Closure ..... 47
10.1.3 Confidentiality and Privacy ..... 47
10.1.4 Future Use of Stored Specimens and Data ..... 48
10.1.5 Key Roles and Study Governance ..... 48
10.1.6 Safety Oversight ..... 51
10.1.7 Clinical Monitoring ..... 52
Preparing for Audits by Regulatory Authorities ..... 52
10.1.8 Quality Assurance and Quality Control ..... 52
10.1.9 Data Handling and Record Keeping ..... 53
Long Term Storage of Forms ..... 53
10.1.10 Protocol Deviations ..... 53
10.1.11 Publication and Data Sharing Policy ..... 53
10.1.12 Conflict of Interest Policy ..... 54
10.2 Additional Considerations ..... 54
10.3 Abbreviations and Special Terms ..... 54
10.4 Protocol Amendment History ..... 55
11 References ..... 56

## STATEMENT OF COMPLIANCE

The trial will be conducted in accordance with International Council on Harmonisation (ICH) Good Clinical Practice (GCP), applicable United States (US) Code of Federal Regulations (CFR), and the National Institute of Dental and Craniofacial Research (NIDCR) Terms and Conditions of Award. The Principal Investigator (PI) will assure that no deviation from, or changes to the protocol will take place without prior agreement from the funding agency and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

### INVESTIGATOR'S SIGNATURE

**Principal Investigator or Clinical Site Investigator:**

Signed:  Date: 01/07/22

Name*: Karin Weber-Gasparoni, DDS, MS, PhD

Title*: Chair and Professor

**Investigator Contact Information:**

Affiliation*: University of Iowa Department of Pediatric Dentistry

Address: 202 Dental Science South, Iowa City, IA 52242-1001

Telephone: (319) 335-7486

Email: karin-weber@uiowa.edu

# 1 PROTOCOL SUMMARY

## 1.1 SYNOPSIS

**Title:** Birth to Three – Cavity Free: Effectiveness of a Psychoeducational Intervention for ECC Prevention

**Grant Number:** UG3DE029443

**Study Description:** This study is considered a Stage II research study according to the NIH Stage Model[1] and will implement an evidence-based behavioral intervention to help expectant mothers develop proper oral health habits early in their future child's life. The central hypothesis is that a theory-based intervention approach facilitated by the self-determination theory (SDT) using videotaped messages and targeted to mothers of high-risk young children will promote an elevated sense of perceived autonomy, competence, and relatedness, which will in turn lead mothers to experience and demonstrate improved self-reported knowledge and behavior concerning their child's oral health. Consequently, their child will have more positive oral health outcomes, indicated by lower levels of caries, dental plaque, and mutans streptococci (MS).

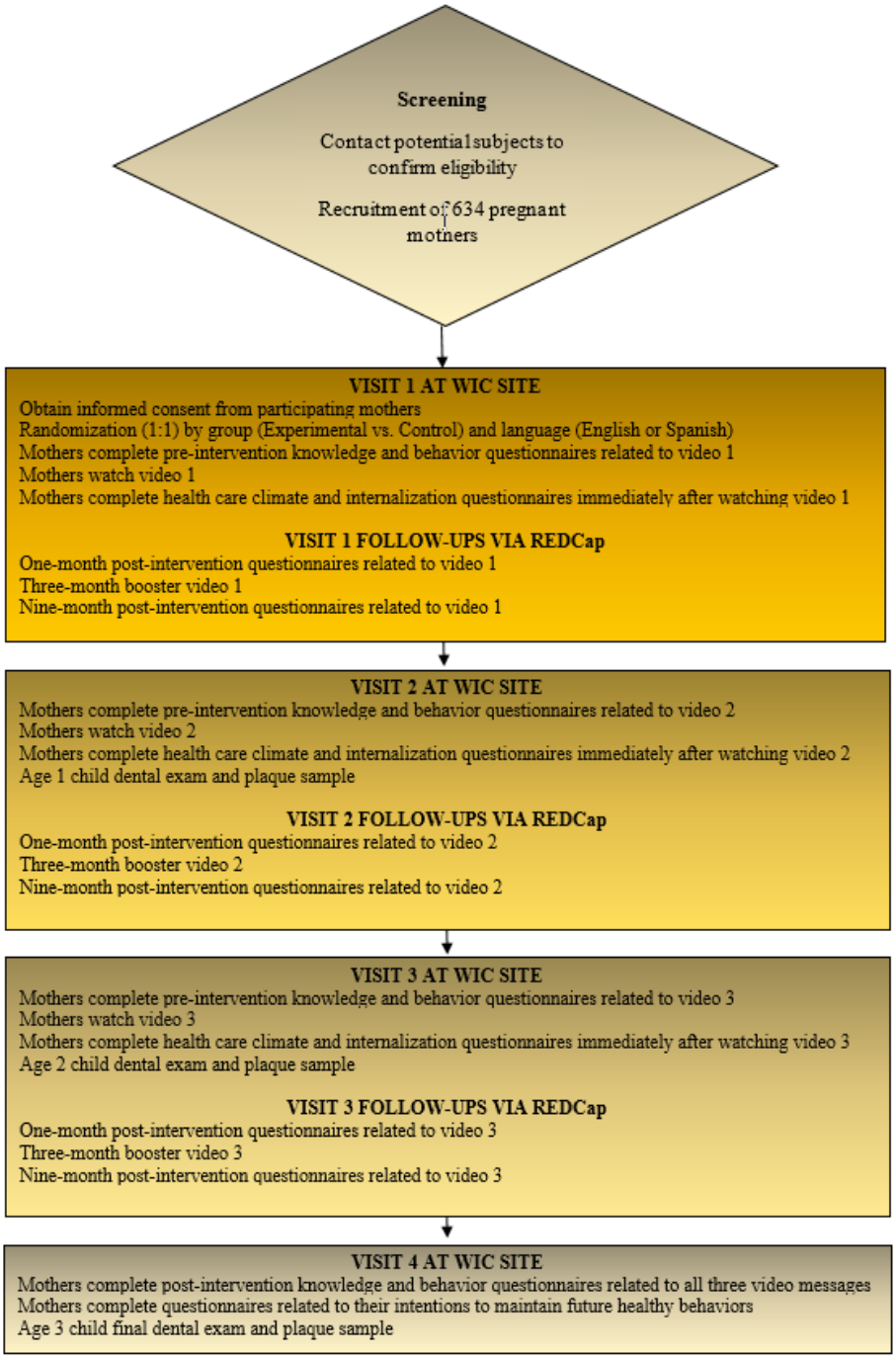
**Objectives*:**

Primary Objective:
1. To test the effectiveness of a multi-component behavioral intervention for pregnant mothers on the subsequent oral health status of their children at ages 12, 24, and 36 months.

Secondary Objectives:
2a. To test the degree to which the intervention produces its effects on children's oral health status through its mediating effects on mothers' changes in self-reported knowledge.
2b. To test the degree to which the intervention produces its effects on children's oral health status through its mediating effects on mothers' changes in behaviors concerning their child's oral health (i.e., oral hygiene habits, dietary habits, use of fluoride, visits to the dentist, lift-the-lip to check for early signs of cavities).
2c. To test the degree to which the intervention improves other indicators of oral health status in children (levels of salivary MS and visible dental plaque scores among the children).

| | | |
|---|---|---|
| **Endpoints:*** | Primary Endpoint: | The primary outcome of interest is children's caries status, as measured by the number of decayed, missing or filled surfaces using the $d_1d_{2\text{-}3}$ mfs scoring method. Both $d_{2\text{-}3}$ and $d_1$ levels, derived from the $d_1d_{2\text{-}3}$mfs caries criteria, will be considered, reflecting numbers of affected (cavitated, missing due to caries or filled) surfaces with and without inclusion of non-cavitated ($d_1$ "white spot") lesions. |
| | Secondary Endpoints: | Secondary outcomes will be changes in maternal knowledge and children's oral health behaviors, as well as lower levels of dental plaque and MS. |
| **Study Population:** | The study sample will consist of 634 pregnant women enrolled from rural and urban Women, Infants and Children (WIC) Supplemental Nutrition Programs in different Iowa counties whose future child will be followed until they are 36 months of age. | |
| **Phase* or Stage:** | Stage II | |
| **Description of Sites/Facilities Enrolling Participants:** | The study sample will be drawn from 12 WIC clinic sites in different counties in Iowa with relatively large Hispanic and African-American populations. | |
| **Description of Study Intervention/Experimental Manipulation:** | Pregnant mothers will be randomly assigned to either an experimental group (Group 1) where mothers will receive autonomy-supportive messages informed by the SDT or a control group (Group 2) where mothers will receive the same oral health care messages delivered using a neutral style. All mothers will be exposed to oral health messages – one during pregnancy, one later when their child is 12 months of age, and one when their child is 24 months of age. Three months after receiving the oral health messages at each time point, mothers will be sent a follow-up booster message. | |
| **Study Duration:*** | 60 months | |
| **Participant Duration:** | Approximately 42 months | |

## 1.2 SCHEMA


Screening
Contact potential subjects to confirm eligibility
Recruitment of 634 pregnant mothers
VISIT 1 AT WIC SITE
Obtain informed consent from participating mothers
Randomization (1:1) by group (Experimental vs. Control) and language (English or Spanish)
Mothers complete pre-intervention knowledge and behavior questionnaires related to video 1
Mothers watch video 1
Mothers complete health care climate and internalization questionnaires immediately after watching video 1
VISIT 1 FOLLOW-UPS VIA REDCap
One-month post-intervention questionnaires related to video 1
Three-month booster video 1
Nine-month post-intervention questionnaires related to video 1
VISIT 2 AT WIC SITE
Mothers complete pre-intervention knowledge and behavior questionnaires related to video 2
Mothers watch video 2
Mothers complete health care climate and internalization questionnaires immediately after watching video 2
Age 1 child dental exam and plaque sample
VISIT 2 FOLLOW-UPS VIA REDCap
One-month post-intervention questionnaires related to video 2
Three-month booster video 2
Nine-month post-intervention questionnaires related to video 2
VISIT 3 AT WIC SITE
Mothers complete pre-intervention knowledge and behavior questionnaires related to video 3
Mothers watch video 3
Mothers complete health care climate and internalization questionnaires immediately after watching video 3
Age 2 child dental exam and plaque sample
VISIT 3 FOLLOW-UPS VIA REDCap
One-month post-intervention questionnaires related to video 3
Three-month booster video 3
Nine-month post-intervention questionnaires related to video 3
VISIT 4 AT WIC SITE
Mothers complete post-intervention knowledge and behavior questionnaires related to all three video messages
Mothers complete questionnaires related to their intentions to maintain future healthy behaviors
Age 3 child final dental exam and plaque sample

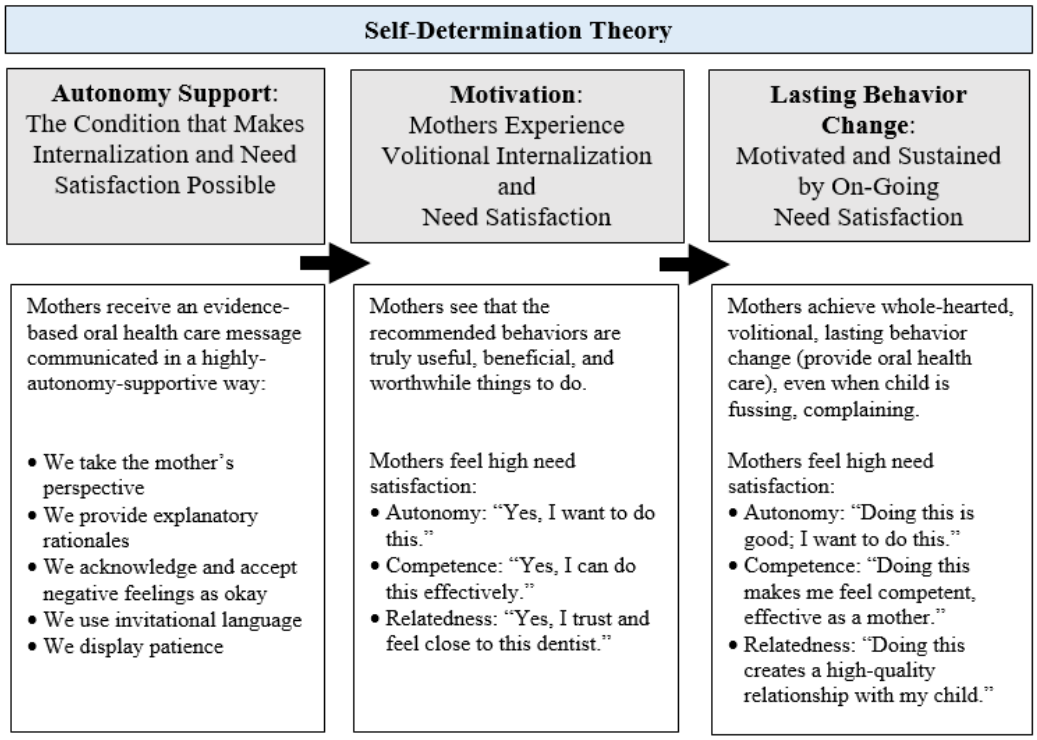
## 1.3 SCHEDULE OF ACTIVITIES

| Study time-points and corresponding activities for ALL study participants in the experimental and control groups | Visit 1 Prenatal | | | | Visit 2 Age 1 to 2 | | | | Visit 3 Age 2 to 3 | | | | Visit 4 Age 3+ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Visit 1 at WIC | 1-Month Follow-up | 3-Month | 9-Month Follow-up | Visit 2 at WIC | 1-Month Follow-up | 3-Month | 9-Month Follow-up | Visit 3 at WIC | 1-Month Follow-up | 3-Month | 9-Month Follow-up | Visit 4 at WIC |
| Informed Consent | ✓ | | | | | | | | | | | | |
| Group randomization | ✓ | | | | | | | | | | | | |
| Mother demographic questionnaire | ✓ | | | | | | | | | | | | |
| Mother knowledge questionnaire | ✓ | ✓ | | ✓ | ✓ | ✓ | | ✓ | ✓ | ✓ | | ✓ | ✓ |
| Mother behavior questionnaire | ✓ | ✓ | | ✓ | | | | | | | | | |
| Intervention videotaped oral health message | ✓ | | | | ✓ | | | | ✓ | | | | |
| Internalization questionnaire | ✓ | | | | ✓ | | | | ✓ | | | | |
| Health care climate questionnaire (HCCQ) | ✓ | | | | ✓ | | | | ✓ | | | | |
| Booster videotaped oral health message | | | ✓ | | | | ✓ | | | | ✓ | | |
| Child plaque sample | | | | | ✓ | | | | ✓ | | | | ✓ |
| Child dental exam: plaque, caries and tooth status recordings | | | | | ✓ | | | | ✓ | | | | ✓ |
| Child behavior questionnaire | | | | ✓ | ✓ | ✓ | | ✓ | ✓ | ✓ | | ✓ | ✓ |
| Mother & child demographic questionnaire | | | | | ✓ | | | | ✓ | | | | ✓ |
| Mother behavior intent questionnaire | | | | | | | | | | | | | ✓ |

# 2 INTRODUCTION

## 2.1 STUDY RATIONALE

Early childhood caries (ECC) is a serious problem, especially among low-income minorities. Although ECC is multifactorial, its primary cause is behavioral.[2] Therefore, the solution, too, should be behavioral. However, healthy behavior change in very young children is a difficult problem that necessarily requires an indirect solution—to help very young children, we need to work with their primary caregivers, usually their mothers. To help mothers provide the high-quality oral health care their young children need, we need to provide a great deal of understanding and support—partly because mothers do not yet know what to do (e.g., "Are sippy cups okay?"), but mostly because their young children routinely and emphatically resist oral health care behaviors (e.g., "I want the M&Ms, not the carrots!"). Many people face similar problems (e.g., smokers, exercisers, dieters), so SDT researchers developed and empirically validated a motivation-based explanatory model to help practitioners solve these difficult problems.[3] The critical ingredients to catalyze volitional, long-lasting behavior change are the motivational experiences of (1) whole-hearted internalization of the recommended behavior change and (2) experiences of need satisfaction (i.e., autonomy, competence, relatedness) to support and maintain that behavior change. The critical social event that makes these motivational conditions possible is an autonomy-supportive relationship.[4] The figure below provides the SDT framework to facilitate internalization and behavior change, and the next section outlines our research strategy to both empirically test this model and translate it into a low-cost behavioral intervention that can be used in WIC clinics and other public health settings across the nation to greatly reduce the burden of ECC among some of the most vulnerable populations.



## 2.2 BACKGROUND

The etiology of ECC is multifactorial. Low socio-economic status is an ECC risk factor,[5] but most ECC risk factors involve health behaviors,[2] such as high frequency of sugar consumption, especially from added-sugar beverages and juice,[6,7] poor oral hygiene,[8-13] and early MS colonization which children acquire from their mothers.[14-17] Caries rates of 35% to 56% have been reported for WIC-enrolled children under the age of three years.[18] Nearly 34% of all 2- to 5-year-old children living under the federal poverty level are affected by caries in the United States, with higher rates among minority children.[19] Behavior-based risk factors (e.g., habitual sugar intake) place children at high risk for ECC. These risk factors are preventable, but the educational preventive messages that have been implemented for pregnant women and mothers have not been effective in increasing mothers' oral-care behaviors or in decreasing their young children's plaque, gingivitis or caries including some that have used videotaped messages.[20,21]

This protocol tests the theory- and evidence-based motivational approach presented in the figure above. This approach and its behavioral strategies come from SDT.[22,23] SDT is relatively unique among theories of motivation due to its focus on the quality, rather than the quantity, of motivation. Central to SDT is the distinction between self-determined or autonomous (i.e., high-quality) and non-self-determined or controlled (i.e., low-quality) forms of motivation.[23,24] Types of motivation differ from one another based on the degree to which actions are (or are not) fully self-endorsed by the individual. Autonomous motivation reflects freely chosen and fully or whole-heartedly self-endorsed reasons for engaging in a behavior, such as "I want to do this because it is important and very useful to me".[25] In contrast, controlled motivation reflects reasons for acting that are not self-endorsed and carry little personal ownership because one feels pressured into doing them, such as "This is something I should do, even though I don't really want to" (internal pressure) or "This is something I have to do; it is required" (environmental pressure).[23]

People acquire autonomous motivation to the extent that they internalize (and take personal ownership over) the recommended behavior change (e.g., brush your teeth, drink water instead of juice). The absence of internalization leaves only controlled motivation, which motivates temporary compliance rather than lasting behavior change.[25] Thus, upon being exposed to a recommended behavior change, the critical motivational event that predicts volitional, lasting behavior change is internalization.[26] The figure on the previous page explains the links among (1) receiving a recommended behavioral change request, (2) volitionally internalizing it to the point that it becomes one's own way of behaving, and (3) lasting, volitional behavior change, even in the face of environmental challenges. The figure begins with autonomy support, which is the adoption of an understanding, mother-focused interpersonal tone.[4] When a health care message is communicated in an autonomy-supportive way, the person offering the health care message works hard to take the mother's point of view (e.g., "How do you feel about this recommendation?"), to provide explanatory rationales for their requests (e.g., "Juice will bathe your child's teeth in sugar; this is why water is better."), to acknowledge and accept the mother's doubts and resistance to the difficult behavior change as okay and as understandable (e.g., "Yes, your child will protest, and the fussing will make this a difficult request for you to carry out."), to rely on invitational language (e.g., "You might consider…"), and to display patience (e.g., "It may take many tries before your child begins to show the first sign of acceptance."). These ways of communicating help the mother discover the value and personal utility within a new way of

behaving, and this sense of value or importance is what gets internalized. In our project, mothers will complete a questionnaire after receiving the videotaped oral health message, and this questionnaire will assess both perceived autonomy support and extent of internalization of the oral health message and its recommendations. Intervention-based research consistently shows that, when people have their autonomy supported while trying to learn and change their behavior, they experience not only greater internalization, but also greater psychological need satisfaction, more autonomous motivation, and a long list of adaptive behaviors, such as engagement, learning, skill development, achievement, prosocial behavior, and adaptive health-promoting behaviors.[4,22,27-31]

As the person tries to work through the internalization experience, experiences of psychological need satisfaction are critical, because need satisfaction is the motivational fuel that drives the internalization process.[32] For a mother to take in a recommended way of behaving as her own and to feel a sense of volition and personal ownership over that behavior, the communicated message needs to provide opportunities to feel the satisfaction of the three psychological needs of autonomy, competence, and relatedness.[23] Autonomy is the psychological need to experience volition, personal ownership, and whole-hearted self-endorsement in one's behavior (e.g., "Yes, I want to do this."). Competence is the psychological need to experience effectance, mastery, and a sense of making progress in one's interactions with the environment (e.g., "Yes, I can do this effectively."). Relatedness is the psychological need to experience warmth, acceptance, closeness, connection, responsiveness, and reciprocal care and concern in one's relationships (e.g., "Yes, I trust and feel close to this dentist.").[23,24] In our project, the questionnaire mothers complete will assess both extent of psychological need satisfaction and intention to engage in the recommended oral health behaviors. Once internalization has occurred, the behavior change needs to be maintained to bear its fruits (e.g., lower levels of dental plaque, MS, and caries). Lasting behavior change is difficult because mothers are busy, tired, and distracted and because their child complains, fusses, and resists the mother's oral health care initiatives. To maintain such lasting behavior change, the mother needs the motivational support of ongoing psychological need satisfaction. While the mother is tired from working all day and trying to brush her fussing child's teeth before bedtime, she critically needs to feel autonomy satisfaction (e.g., "Doing this is good; I want to do this."), competence satisfaction (e.g., "Doing this makes me feel competent, effective as a mother."), and relatedness satisfaction (e.g., "Doing this creates a high-quality relationship with my child."). These experiences of need satisfaction motivationally support continual internalization and ongoing, persistent behavior change. In our project, mothers will complete a series of follow-up questionnaires (i.e., 6 months, 9 months) to assess the maintenance (and even increases) in their experiences of need satisfaction and intentions to engage in the previously recommended oral health care behaviors. In the medical field, autonomy-support facilitated perceived competence and autonomous motivation for long-term health behavior change, which improved (a) adherence to exercise and subsequent weight loss among morbidly obese patients for over 23 months,[27] and obese females for over 3 years;[33] (b) long-term medication adherence;[34] (c) self-management, glycemic control, quality of life, and physiological outcomes among patients with Type 2 diabetes;[24,35] and (d) medication taking and 6-month tobacco cessation[36] and 24- month prolonged tobacco abstinence.[37] In the dental field, autonomy-support led to satisfaction of psychological needs, resulting in patients' decreased plaque and gingivitis levels,[38, 39] improved home brushing and flossing,[38,40] increased fluoride

use,[41] decreased frequency of sugar consumption,[41] more positive dental health attitudes,[38] and higher dental clinic attendance.[40]

We believe that the SDT-based model proposed for this study provides an autonomy-supportive oral health care message targeted to mothers of high-risk children and therefore will promote greater autonomy, competence, and relatedness psychological need satisfaction. Because of this experience of need satisfaction while exposed to the videotaped healthcare message, mothers will be significantly more likely to identify with the message, internalize it, and accept its recommendations as their own. That acceptance and ownership will promote the mothers' willingness to increase their oral health care knowledge, increase their willingness and intentions to engage in constructive oral health care behaviors, increase their actual oral health care parenting behaviors, and increase their parenting self-efficacy to carry out those constructive oral health care behaviors in a way that will produce desired oral health benefits for their children. According to SDT, the greater extent to which the autonomy-supportive message allows mothers to experience autonomy support and volitional internalization, the more positive will be the mothers' post-message oral health care motivation (need satisfaction, autonomous motivation), knowledge and behavioral care for their children. These gains in the mother's oral health care motivation, knowledge, behaviors, and self-efficacy will be the active ingredients during mother-child interactions that produce longitudinal gains in the children's oral health outcomes, as evidenced by lower levels of dental plaque, MS, and caries. In other words, mothers of high-risk children who receive our videotaped autonomy-supportive messages, compared to mothers of high-risk children who receive only a videotaped neutral message, will gain greater capacity and skills to provide their children with high-quality oral health care.

The four-fold reasons why this SDT-based autonomy-supportive intervention will be effective (will increase mothers' capacity to provide high-quality oral health care) are because (1) the recommended parenting knowledge and behavior will be communicated in a highly autonomy-supportive way (i.e., take the mother's perspective, encourage initiative, provide explanatory rationales, acknowledge and accept negative affect), (2) mothers will experience this autonomy-supportive context as deeply need satisfying (i.e., mothers will feel high autonomy, competence, and relatedness satisfaction while learning about high-quality oral health care), (3) this experience of high need satisfaction will allow mothers to identify personally with the parenting message, internalize both the message and the recommended parenting behaviors, and accept the message and parenting behaviors as their own, and (4) mothers will learn how to apply all these constructive oral health care behaviors (e.g., daily brushing, no sugared beverages) toward their child's oral health in an effective way. Given that the autonomy-supportive messages (videotape) help mothers gain a greater capacity to provide their children with high-quality oral health care (i.e., greater knowledge and parenting behaviors), mothers will be significantly more able to prevent caries in their children at ages 12, 24, and 36 months (the study's primary outcomes), as well as promote their children's improved oral hygiene (i.e., less plaque and less MS; the study's secondary outcomes).

## 2.3 RISK/BENEFIT ASSESSMENT

### 2.3.1 KNOWN POTENTIAL RISKS

The physical risks for children and mothers involved in this research are minimal and unexpected. Children will participate in a dental examination and plaque sampling at three time points (at approximately ages 12, 24, and 36 months). These exams and plaque sampling will be conducted by oral health providers trained in conducting dental exams on infants and toddlers, including managing uncooperative behavior during exams. While unlikely and rare, there is a risk of infection as a result of these procedures. Standard infection control procedures will be followed to minimize infection risk.

Most other risks also are minimal and unexpected. As with all clinical research, breach of confidentiality of subject data is a risk, however, there will be study procedures in place to minimize this risk. Specifically, the risk to subject confidentiality will be minimized by assigning unique identification numbers to all subjects, and all study documents will use only these numbers to identify subjects. In this way, the name and contact information for all subjects will not be directly matched to the study data. A document that matches the contact information with study identification numbers will be maintained separately, with only the PI and research staff having access to this document. All study data will be stored on the secure server at the UI College of Dentistry. The data will be periodically backed up. A separate password will be created for the database and changed periodically. Only authorized individuals (e.g., PI and Clinical Trial Research Associate (CTRA)) will have access to the database. Paper-based questionnaires and other documents will be securely stored in locked cabinets in a locked office. Results of the study and study data will only be reported in aggregate form, so that individual subjects are not identifiable. A data safety monitoring plan will be in place to protect human subjects and assure confidentiality and data security. Additionally, participating women may feel uncomfortable answering some of the questionnaire questions, for example questions about feeding practices that do not adhere to the recommendations of the videotaped messages. Mothers will be reminded that their study participation is voluntary, and they may elect to skip any question(s) they do not feel comfortable answering.

The one risk that is expected is that of children being upset and uncooperative during the dental exam and plaque collection procedures, given the young age of child participants (approximately 12 months – 36 months of age). Study procedures are designed to maximize the comfort of children and mothers during these clinical procedures. Specifically, mothers will be present at all times during the child's oral examination and it will be reinforced verbally that all procedures accomplished with their child are simple and safe. The tell-show-do technique will be used during all procedures in order to help relax the child and obtain his or her cooperation. The technique is simple and dictates that, before anything is done, the child is told what will be done and then shown by some sort of simulation exactly what will happen before the procedure is started. A puppet stuffed animal will be used to simulate the dental procedures to be done with the child. There are no alternative procedures; however, mothers will be assured that participation in this study is strictly voluntary. They and their children can choose to decline any aspect of the study at any time and may discontinue their participation at any time without any negative consequences.

### 2.3.2 KNOWN POTENTIAL BENEFITS

Participating children will receive dental screenings by University of Iowa (UI) providers who are authorized, trained, and calibrated to make caries diagnosis. Mothers will receive oral and written information about their children's caries status when they are ages 12, 24, and 36 months.

### 2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

The potential benefits of the study outweigh the risks.

## 3 OBJECTIVES AND ENDPOINTS

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS | PUTATIVE MECHANISMS OF ACTION |
|---|---|---|---|
| Primary | | | |
| To test the effectiveness of a multi-component behavioral intervention for pregnant mothers on the subsequent oral health status of their children at ages 12, 24, and 36 months. | The primary outcome of interest is caries status. Caries status at each of the annual examinations will be expressed in terms of the number of decayed, missing or filled surfaces using the $d_1d_{2-3}$mfs scoring method, as well as crude, net and adjusted incidence rates.[42,43] Both $d_1d_{2-3}$mfs and $d_1$mfs categories derived from the $d_1d_{2-3}$mfs caries criteria will be considered, reflecting numbers of affected cavitated ($d_{2-3}$), missing due to caries or filled) surfaces with and without inclusion of non-cavitated ($d_1$ "white spot") lesions. | The caries criteria for scoring dental caries for the children were developed by members of the Iowa Fluoride Study[44] and successfully adapted for caries epidemiological exams in young children in 3 NIDCR Disparities Centers (Universities of California San Francisco, Colorado Denver and Boston).[45-49] | According to SDT, the greater the extent to which the autonomy-supportive message allows mothers to experience autonomy support and volitional internalization, the more positive will be the mothers' post-message oral health care motivation (need satisfaction, autonomous motivation), knowledge, and behavioral care for their children. These gains in the mother's oral health care motivation, knowledge, behaviors, and self-efficacy will be the active ingredients during mother-child interactions that produce longitudinal gains in the children's oral health outcomes as evidenced by *lower levels of caries*. In other words, mothers of high-risk children who receive our videotaped autonomy-supportive message, compared to mothers of high-risk children who receive only a videotaped neutral message, will gain greater capacity and skill to provide their children with high- |

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS | PUTATIVE MECHANISMS OF ACTION |
|---|---|---|---|
| | | | quality oral health care. Consequently, their children will have lower numbers of decayed, missing or filled surfaces. |
| Secondary | | | |
| (2a) To test the degree to which the intervention produces its effects on children's oral health status through its mediating effects on mothers' changes in self-reported knowledge. | (2a) Maternal knowledge will be assessed through a series of questions using 5-point Likert-type scale with anchors of "strongly disagree" to "strongly agree" on topics such as early childhood caries etiology (i.e., bacteria transmission), dietary habits (i.e., bottle/breast feeding, use of sippy-cup, juice consumption, snacks, etc.), oral hygiene habits (i.e., time of brushing, person responsible for brushing the child's teeth, fluoride toothpaste use, etc.). These questions will be specific to the messages given at each of the three videotaped oral health messages time points. The pre-intervention self-reported knowledge questionnaires will be administered prior to watching the video | (2a) The same questionnaires were used and validated in several previous research projects from the research team.[10-13,50-55] | (2a) According to SDT, the greater the extent to which the autonomy-supportive messages allow mothers to experience autonomy support and volitional internalization, the more positive will be the mothers' post-message oral health care motivation (need satisfaction, autonomous motivation) *knowledge*. In other words, mothers of high-risk children who receive our videotaped autonomy-supportive message, compared to mothers of high-risk children who receive only a videotaped neutral message, will demonstrate greater increases in knowledge scores. |

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS | PUTATIVE MECHANISMS OF ACTION |
|---|---|---|---|
| | messages at visits 1, 2 and 3, and the post-intervention knowledge questionnaires will be administered at one- and nine-month follow-ups.<br>*At the final visit (Visit 4), knowledge questions will assess the key topics discussed previously at all three time points. | | |
| (2b) To test the degree to which the intervention produces its effects on children's oral health status through its mediating effects on mothers' changes in behaviors concerning their child's oral health (i.e., oral hygiene habits, dietary habits, use of fluoride, visits to the dentist, lift-the-lip to check for early signs of cavities) | (2b) Maternal behaviors toward the child's oral health will be assessed through a series of questions (i.e., visit to the dentist, detailed dietary and oral hygiene habits, etc.) that are pertinent to the behaviors recommended at each of the three videotaped oral health message time points. The pre-intervention self-reported behavior questionnaires will be administered prior to watching the video messages at visits 1, 2 and 3, and the post-intervention behavior questionnaires will be administered at one- | (2b) The same questionnaires were used and validated in several previous research projects from the research team.[10-13,50-55] | (2b) According to SDT, the greater the extent to which the autonomy-supportive message allows mothers to experience autonomy support and volitional internalization, the more positive will be the mothers' post-message oral health care motivation (need satisfaction, autonomous motivation), *behavioral care for their children*. In other words, mothers of high-risk children who receive our videotaped autonomy-supportive messages, compared to mothers of high-risk children who receive only videotaped neutral messages, will demonstrate more positive changes |

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS | PUTATIVE MECHANISMS OF ACTION |
|---|---|---|---|
| | and nine-month follow-ups.<br>*At the final visit (Visit 4), behavior questions will assess the key topics discussed previously at all three time points. | | regarding behaviors towards their children's oral health, such as more positive oral hygiene and dietary habits, use of fluoride, visits to the dentist, lift-the-lip to check for early signs of cavities, etc. |
| (2c) To test the degree to which the intervention improves other indicators of oral health status in children (levels of salivary MS[a] and visible plaque[b] scores among the children). | (2c[a]) Plaque samples will be obtained from all participating children at visits 2, 3 and 4. Samples will be obtained by using sterile cotton swabs; all tooth surfaces will be swabbed. Cotton swabs will be immersed in sterile transport fluids and kept cold for transport to the microbiology labs. Numbers of bacteria will be derived for each sample from these media following the standard matrix counting methodology of the spiral plating system. | (2c[a]) The same protocol was used and validated in several previous research projects from the research team.[10-13,50-55] | (2c[a]) According to SDT, the greater the extent to which the autonomy-supportive message allows mothers to experience autonomy support and volitional internalization, the more positive will be the mothers' post-message oral health care motivation (need satisfaction, autonomous motivation), knowledge and behavioral care for their children. These gains in the mother's oral health care motivation, knowledge, behaviors, and self-efficacy will be the active ingredients during mother-child interactions that produce longitudinal gains in the children's oral health outcomes as evidenced by *lower levels of salivary MS*. In other words, mothers of high-risk children who receive our videotaped autonomy-supportive messages, compared to |

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS | PUTATIVE MECHANISMS OF ACTION |
|---|---|---|---|
| | | | mothers of high-risk children who receive only a videotaped neutral messages, will gain greater capacity and skill to provide their children with high-quality oral health care. Consequently, their children will have lower levels of salivary MS. |
| | (2c[b]) Each child will be examined at 12, 24 and 36 months of age (visits 2, 3 and 4) for visible plaque by one of the dentist-examiners using a knee-to-knee technique. Visible plaque will be assessed first and recorded as present or absent for the maxillary and mandibular incisors and molars. The number of maxillary and mandibular incisors and molars with plaque will also be recorded. | (2c[b]) The same protocol was used and validated in several previous research projects from the research team. [10-13,50-55] | (2c[b]) According to SDT, the greater the extent to which the autonomy-supportive message allows mothers to experience autonomy support and volitional internalization, the more positive will be the mothers' post-message oral health care motivation (need satisfaction, autonomous motivation), knowledge and behavioral care for their children. These gains in the mother's oral health care motivation, knowledge, behaviors, and self-efficacy will be the active ingredients during mother-child interactions that produce longitudinal gains in the children's oral health outcomes as evidenced by *lower levels of visible plaque*. In other words, mothers of high-risk children who receive our |

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS | PUTATIVE MECHANISMS OF ACTION |
|---|---|---|---|
| | | | videotaped autonomy-supportive messages, compared to mothers of high-risk children who receive only a videotaped neutral messages, will gain a greater capacity and skill to provide their children with high-quality oral health care. Consequently, their children will have lower levels of visible plaque. |

# 4 STUDY DESIGN

## 4.1 OVERALL DESIGN

This UH3 clinical trial study constitutes a Stage II research according to the NIH Stage Model.[4] The study design specifies a two-arm, randomized controlled clinical trial to assess the effectiveness of autonomy-supportive videotaped oral health messages informed by SDT as a means of preventing ECC, as compared to the effects of exposure to neutral messages also delivered via videotape. The intervention is intended for use in public health settings attended by high-caries risk groups, and the proposed UH3 clinical trial will be conducted at several WIC clinic sites in different rural and urban counties in Iowa with relatively large Hispanic and African-American populations.[51,52]

The study sample will consist of 634 pregnant women whose future children will be followed until they are 36 months of age. Pregnant women, between 12 and 36 weeks of the gestational period, 18 to 45 years old, and with no intention to move away in the next four years will be eligible to participate in the study. Recruitment will occur anywhere between 12 to 36 weeks of gestation. However, study interventions will only start between 16 to 36 weeks of gestation. If a pregnant woman is recruited between 16 to 36 weeks of gestation, the study procedures can begin immediately. If the woman is recruited between 12 to 15 weeks of gestation, we will schedule her an initial study visit for later, that is between 16 to 36 weeks of the gestation period. At their first study visit, informed consent will be obtained. After informed consent, they will be randomly assigned to one of two study groups: Group 1 (experimental (SDT) group) and Group 2 (neutral control group). The primary outcome of interest will be children's caries status. Secondary outcomes will be changes in children's oral health behaviors conducive to better oral hygiene and dietary habits, as well as lower levels of dental plaque and MS.

The central hypothesis is that a theory-based intervention approach using videotaped messages and targeted to mothers of high-risk young children will promote an elevated sense of perceived autonomy, competence, and relatedness, which will in turn lead mothers to experience and demonstrate improved self-reported knowledge, behavioral intention and subsequent behavior concerning their child's oral health. Consequently, their child will have more positive oral health outcomes, such as lower levels of caries, dental plaque, and MS. We predict that the theory-based intervention will enhance mothers' oral health care knowledge (Hypothesis 1) and behavior toward their oral health and their child's oral health (Hypothesis 2), relative to neutral messages, also delivered via videotapes. In addition, these hypothesized benefits will apply to both short-term (one-month) and long-term (nine-month) effects across each time point (prenatal, Age 1-2, Age 2-3, Age 3+).

## 4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The strategy of providing caretakers with autonomy support has been shown to produce very large effect sizes across multiple domains.[23,25,56] There is a need to evaluate the effectiveness of a theory-based intervention to alleviate the ECC burden using a psychological theory of motivation, such as SDT, proven useful in promoting behavior change in several domains.[3,24,25,34]

## 4.3 JUSTIFICATION FOR INTERVENTION

The mode of our intervention delivery is through videotaped oral health messages presented through a link on a tablet at the WIC clinic sites or through a participant's smart phone between site visits. This intervention delivery provides a cost-effective behavioral approach targeted to ECC prevention and does not depend on the availability of either dental and/or medical professionals to deliver the oral health messages. Empirical research, including our own preliminary work, has shown this particular video-based autonomy supportive intervention (SDT) to be accepted by WIC mothers and effective in ECC-prevention.[50] Our prior focus groups reported that the video length along with images and messages were both appealing and understood by the WIC mothers. The mothers also felt the videotaped oral health messages represented different ethnic groups and reflected their own life experiences.

The literature supports supplemental follow-up activities in boosting the original intervention experience to reinforce the oral health message.[57] Therefore, mothers will receive a 3-month booster message via link through their smart phone after each oral health message received at their study WIC visits 1, 2 and 3. Viewing of the 3-month booster message is optional.

The minimum-acceptable participation in order to have evaluable data on the study primary outcome would be the first and last visits. At the last visit, children will be examined for their caries status, therefore participation in this visit will be essential to assess the overall effectiveness of our intervention on ECC prevention. Ideally, the participants will complete the four WIC site visits, as well as study activities at 1-, 3- and 9 months post WIC visits to access their changes in knowledge and behavior towards their child's oral health, as well as retention and continued use of the information presented at each intervention.

## 4.4 END-OF-STUDY DEFINITION

The end of the study is defined as the date when the last participating mother-child dyad completes study activities for the last visit (Visit 4).

# 5 STUDY POPULATION

## 5.1 INCLUSION CRITERIA

1) WIC-participating pregnant women who are 18 to 45 years old.
2) Between 12 and 36 weeks of the gestational period.
3) Able to speak, understand and read English or Spanish
4) No intention to move away in the next 4 years.

## 5.2 EXCLUSION CRITERIA

3) Mothers who deliver their child prior to their first study intervention visit.

## 5.3 LIFESTYLE CONSIDERATIONS

NA

## 5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in this study and do not meet one or more inclusion criteria and/or do meet the exclusion criteria for participation in this trial (screen failure). Examples include a pregnant woman giving birth prior to the first intervention visit or not being fluent in either English or Spanish languages, in which case she would no longer be eligible for the study. Each potential screen failure will need to be determined on a case-by-case basis.

## 5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

We plan to assess our recruitment rate during months three through 12 after the clinical trial starts. If the pace of recruitment is slow, we will increase recruitment days, advertise our study more aggressively through posters and media avenues, recruit participants from additional WIC sites, and/or consider increasing the incentives given to participating mothers and children. We will assess our retention rates annually at months 12, 24 and 36 of follow-up. If our follow-up exam rate is below the expectancy, then we plan to adopt the same methods described above for recruitment, as well as conduct the study at WIC sites that provide services on Saturday mornings. With four dental examiners, we will be able to increase the number of exam days, allowing mothers more flexibility in scheduling their study visits, improving retention and helping us finish the study on time.

Study staff will recruit subjects at all participating WIC sites on targeted clinic days. The CTRA and research assistants (RAs) will work to create schedules whereby specific days are chosen based on WIC site schedule and attendance patterns in order to maximize the number of WIC clients successfully recruited. Verbal and written information will be provided to prospective participants, and upon obtaining consent, subjects will be enrolled in the study. In some cases, for pregnant women who express interest but decline enrollment at that time, contact information will be gathered and follow-up emails/text messages and telephone calls made in an attempt to secure their enrollment in the study. In addition to the recruitment described above, WIC study staff will provide an informational brochure to each client who meets inclusion criteria, with WIC staff collecting names, home addresses/telephone numbers, and emails from interested

women (after the women give permission for sharing the information). The WIC staff will then forward this information to study staff who will call the mothers directly to 1) provide a brief overview of the study and introduce the potential risk and benefits of participation, 2) determine interest in study participation, and 3) if they are interested, schedule an initial appointment, at which time formal enrollment will take place and informed consent obtained. The study brochures and posters will be placed at the WIC sites will provide a QR code linking to a contact sheet that mothers can directly fill out to allow study team members to follow-up and contact them.

In order to increase retention, every attempt will be made to maintain contact with all study participants during the clinical trial period through bi-annual study newsletters, multiple phone calls, texts, and emails, along with personal cards to provide valuable communication and continued support with the participants (i.e., congratulate mothers on the baby's birth, mother's and child's birthdays, Mother's Day, thank you notes, etc.). We will create social media contacts through a Birth to Three Cavity Free Facebook study account, and ensure all participants are sent individual, direct messages to prevent information sharing between participants. All of these efforts are crucial to maintaining our cohort of participants.

For all study participants, phone, text, email and/or mail contacts will be made to schedule forthcoming assessment appointments and keep participants engaged in the study. Contacts will include newsletter with updates about the study, as well as thanking the participants. In order to enhance continuing participation in this study, the participants will be verbally encouraged to combine their regular WIC appointments with their visits for this study. In addition, a phone call and text message through REDCap™ (Research Electronic Data Capture) will occur to every participant one week prior to each scheduled appointment to remind them about the time and location, as well as a text message a day before to confirm their appointment attendance. If a WIC appointment is missed, mothers will be allowed up to 2 months to reschedule any of the in-person WIC site visits. If mother's misses the 2-month time window, she will not be able to continue the follow-up questionnaires until the next yearly WIC visit.

Mother's will have up to eight weeks to complete the one- and nine-month questionnaires via REDCap™, with weekly reminders to complete them. If mothers do not complete the questionnaires after the first three reminders, REDCap™ will notify the study team, and an RA will contact the mother to complete the questionnaires. Non-responders will also be mailed paper copies of the questionnaires with a prepaid and self-addressed envelope to return once completed.

Due to the time spent at each study visit (~1.5 hours) to complete all study procedures (i.e. consent forms, pre- and post-questionnaires, view video messages, dental examination, etc.), incentives for the subjects will include dispensing of toothbrushes, fluoride toothpaste and a small toy at each visit for the study children and a gift card to the study mothers. Monetary gift cards will be given to participants after completing study visits and returning questionnaires at each one- and nine-month time points as it follows:

Visit 1 (Prenatal): $50
1-month follow-up questionnaires: $20

9-month follow-up questionnaires: $20
Visit 2 (age 1 to 2): $75
1-month follow-up questionnaires: $20
9-month follow-up questionnaires: $20
Visit 3 (age 2 to 3): $100
1-month follow-up questionnaires: $20
9-month follow-up questionnaires: $20
Visit 4 (age 3+): $125

If needed, a no-cost extension to allow more time to complete the study will be sought.

# 6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

## 6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

### 6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

This is a two-arm, randomized controlled clinical trial (NIH Stage II Research Model) [4] to assess the effectiveness of autonomy-supportive videotaped oral health messages informed by SDT as a means of preventing ECC, as compared to the effects of exposure to neutral messages also delivered via videotape. The intervention is intended for use in public health settings attended by high-caries risk groups. Enrollment may take as long as 18 months but is likely to require significantly fewer months to meet recruitment goals.[54] Study participation will last approximately 3½ years. Subjects, clinical examiners and statistical analysts will be blinded with respect to treatment allocation; care will be taken to maintain allocation concealment. Treatment allocation will be based upon a randomization schedule (to groups 1 or 2 provided by REDCap™). In addition to the study CTRA, RAs will not be blinded, so that they can deliver the assigned intervention as a supervised exposure to prevent contamination, as a further measure to ensure rigor and transparency.

### 6.1.2 ADMINISTRATION AND/OR DOSING

- Mothers will be randomly assigned to either an experimental (SDT) group (Group 1) where mothers will receive SDT-informed autonomy-supportive messages or a control (neutral) group (Group 2) where mothers will receive the same oral health care messages delivered using a neutral style.
- All mothers will be exposed to a series of three videotaped oral health messages - during pregnancy, and then when their child is 12 and 24 months of age.
    - The first videotaped message will be shown during the prenatal period and will cover a variety of oral health topics regarding the pregnant women's own oral health, the impact of their general and oral health on their future child's oral health, and oral health issues focused on specific needs for children 0 to 12 months of age.
    - The second videotaped message will be shown when the child is 12 months of age and cover oral health issues focused on specific needs for children 12 to 24 months of age.
    - The third videotaped message will be shown when the child is 24 months of age and cover oral health issues focused on specific needs for children 24 to 36 months of age.
- The oral health messages in all three videos for the experimental group (Group 1) will be informed by the SDT. All videos for the experimental (SDT) group (Group 1) will cover a variety of oral health topics: the impact of the mother's oral health on their children's oral health, process of tooth decay, oral hygiene practices, dietary habits that affect caries susceptibility, and checking the child's teeth for early signs of cavities (white spot lesions). Throughout the videos, motivation messages will address the harm of inappropriate oral hygiene and dietary habits, challenges mothers face in caring for their

child's oral health, and tips for positive oral health practices. These messages will be communicated in an autonomy-supportive way.

- All videos for the control (neutral) group (Group 2) will cover the same dental content presented in the videotaped messages for the experimental (SDT) group (Group 1); however, the message will be delivered using a neutral style and will be simply informative.
- Prior to watching the videotaped messages at visits 1, 2 and 3, participating women from both groups will complete a series of pre-intervention questionnaires regarding their own oral health and their (future) child's oral health. The questionnaires will include information regarding the mother's (1) demographics; (2) perceptions and status of their own oral health; and (3) pre-intervention self-reported knowledge and behavior concerning their own oral health (dietary/oral hygiene behaviors, frequency of visits to the dentist, etc.), as well as concerning their child's oral health (child's dietary/oral hygiene habits, etc.).
- Immediately after viewing the videotaped oral health messages at visits 1, 2 and 3, participating women from both groups will complete two additional questionnaires to assess their perceptions of the degree of autonomy support of the videotaped messages. One questionnaire will assess the mothers' perceived feelings of autonomy, relatedness, and competence ("health care climate questionnaire"), and the other will assess the mother's internalization of the videotaped message (i.e., the degree to which mothers understood, agreed with, and perceived the oral health message as helpful and useful to them ["internalization questionnaire"]).
- SDT proposes that, if the participating woman has internalized the message, the changes should be evident within a short period of time.[7] Thus, participating women from both groups will be asked to complete post-intervention questionnaires at *one-month follow-up* after viewing the videotaped messages at visits 1, 2 and 3 designed to assess mothers' changes in self-reported knowledge and subsequent oral health behavior towards their child's oral health. According to the informed consent approved by the UI IRB, "You (study participant) may feel uncomfortable in answering certain questions and you can choose to decline any aspect of the study at any time. You and your child may discontinue participating at any time without any negative consequences." Therefore, participants may choose not to complete the one-month follow-up questionnaires.
- Booster messages will be sent to mothers at *three-month follow-up* after viewing the videotaped oral health messages at visits 1, 2 and 3 to help them overcome the difficulties of adopting the suggested behaviors. The booster messages for mothers of Group 1 will be autonomous-supportive, while neutral for mothers of Group 2. Viewing of the 3-month booster message is optional.
- In order to assess long-term behavioral changes, all study mothers will be asked to complete again the post-intervention questionnaires at *nine-month follow-up* after viewing the videotaped messages at visits 1, 2 and 3. According to the informed consent approved by the UI IRB, "You (study participant) may feel uncomfortable in answering certain questions and you can choose to decline any aspect of the study at any time. You and your child may discontinue participating at any time without any negative consequences." Therefore, participants may choose not to complete the nine-month follow-up questionnaires.

- Each child will be examined at 12, 24 and 36 months of age (visits 2, 3 and 4) for visible plaque and dental caries by one of the examiners who will be blinded to participants' group assignment. We will utilize the $d_1d_{2\text{-}3}$ mfs caries criteria for scoring dental caries for the children.
- Plaque samples will also be obtained from all participating children at visits 2, 3 and 4. Numbers of MS will be derived for each sample through the standard matrix counting methodology of the spiral plating system. Plaque samples will be obtained by using sterile cotton swabs; all teeth surfaces will be swabbed. Cotton swabs will be immersed in sterile transport fluids and kept cold for transport to the microbiology labs. All laboratory procedures will be done by an experienced research scientist and under the overall guidance of Dr. Drake, Professor of Microbiology & Infectious Diseases. Dr. Drake will routinely audit the database and reconcile it to a logbook that has the identification numbers for the samples stored in the ultralow freezer on a monthly basis.

**Detailed Description of the Study Intervention**

This is a two-arm, randomized controlled clinical trial that will compare the efficacy of autonomy-supportive videotaped oral health messages framed by SDT to more traditional neutral videotaped messages. We intent to recruit pregnant mothers enrolled in Iowa Women, Infants and Children (WIC) Supplemental Nutrition Programs and follow them until their future child is 36 months old. The primary outcome of interest will be children's caries status. Secondary outcomes will be changes in children's oral health behaviors conducive to better oral hygiene and dietary habits, as well as lower levels of dental plaque and MS.

Assuming an effect size (treatment difference) of 1.1 (standard deviation 3.45) for the number of cavitated, missing or filled lesions, Type I error level of 0.05, and 80% power, required sample size is 156 children per group at the three-year follow-up. Given enrollment of 317 mother-child dyads for each group (SDT video or neutral control), and a conservative annual attrition rate of 21%, 156 dyads per group (312 total) would be expected to complete three-year follow-up. Subjects, clinical examiners, and statistical analysts will be blinded with respect to treatment allocation. A block-level randomization scheme with a 1:1 allocation ratio will be used to determine interventions for individuals. Random block sizes of 2, 4, and 6 will be used to create the randomization scheme. Randomization will be stratified on primary language and site to ensure balance between the intervention groups. There will be 12 possible sites in the study. In addition to the CTRA, RAs will not be blinded so that they can deliver the assigned intervention.

Enrollment may take as long 18 months. Study participation will last approximately 42 months. We intent to enroll 317 pregnant mothers for each group: Group 1 (experimental - SDT)/Group 2 (neutral control). There will be four visits at the WIC clinics with three follow-ups after each WIC site visit. Outcomes will be measured at each study time points. Data will be collected in person at the WIC site visits and through completion of questionnaires through REDCap™ at follow-ups after each WIC visit. Visit 2, 3 and 4 will be scheduled based upon the child's DOB and will take place when the child is approximately 12, 24 and 36 months of age. Children will be examined (visits 2, 3 and 4) for visible plaque and dental caries by one of the study examiners who will be blinded to the participant's group allocation. Plaque samples will also be obtained from all participating children at visits 2, 3 and 4. Numbers of MS will be derived for each sample through the standard matrix counting methodology of the spiral plating system.

**Detailed Description of the Study Procedures**

The table below details the study procedures:

| Visit | Time | Window | Purpose and Activities | Location |
|---|---|---|---|---|
| 1.0 | Visit 1 | Day 0 | Enrollment, informed consent, group randomization, pre-intervention questionnaires, video 1 message, post-video HCCQ and Internalization questionnaires | WIC Clinic |
| 1.1 | 1 month | +8 weeks | Post-intervention questionnaires | Links via REDCap™ |
| 1.2 | 3 months | +6 months | Booster video 1 message | Links via REDCap™ |
| 1.3 | 9 months | +8 weeks | Post-intervention questionnaires | Links via REDCap™ |
| 2.0 | Visit 2 | 1 year ±2 months | Pre-intervention questionnaires, video 2 message, post-video HCCQ and Internalization questionnaires, child's dental exam and plaque sample | WIC Clinic |
| 2.1 | 1 year & 1 month | +8 weeks | Post-intervention questionnaires | Links via REDCap™ |
| 2.2 | 1 year & 3 months | +6 months | Booster video 2 message | Links via REDCap™ |
| 2.3 | 1 year & 9 months | +8 weeks | Post-intervention questionnaires | Links via REDCap™ |
| 3.0 | Visit 3 | 2 years ±2 months | Pre-intervention questionnaire data, video 3 message, post-video HCCQ and Internalization questionnaires, child's dental exam and plaque sample | WIC Clinic |
| 3.1 | 2 years & 1 month | +8 weeks | Post-intervention questionnaires | Links via REDCap™ |
| 3.2 | 2 years & 3 months | +6 months | Booster video 3 message | Links via REDCap™ |
| 3.3 | 2 years & 9 months | +8 weeks | Post-intervention questionnaires | Links via REDCap™ |
| 4.0 | Visit 4 | 3 years ±2 months | Post-intervention questionnaires, child's dental exam and plaque sample | WIC Clinic |

## 6.2 FIDELITY

### 6.2.1 INTERVENTIONIST TRAINING AND TRACKING

We will hold staff training sessions led by team experts to ensure accurate and complete data collection, storage, transportation, processing, and analyses (e.g., questionnaires, plaque collection). We will have backup plans to ensure data collection in case unanticipated problems arise (for instance, paper forms instead of REDCap™ for survey data collection due to internet issues). Participant-level checklists will be used to ensure that all necessary data elements are collected at each data collection visit. All data documents will be reviewed for completeness within 24 hours so that relevant corrections or unintentionally missing data can be collected. Data accuracy will be confirmed at the level of data collection by the CTRA. Any staff with

consistent quality issues concerning data collection will receive feedback and be re-trained, as necessary. Staff training will include hands-on training, practice sessions, validation exercises to ensure accuracy, and certification. The CTRA will provide ongoing feedback to data collectors regarding data quality.

## 6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

A block-level randomization scheme with a 1:1 allocation ratio will be used to determine interventions for individuals. Random block sizes of 2, 4, and 6 will be used to create the randomization scheme. Randomization will be stratified on primary language and site to ensure balance between the intervention groups. Subjects, clinical examiners, and data analyst will be blinded with respect to treatment allocation; care will be taken to maintain allocation concealment. However, the study CTRA and RAs will not be blinded so that they can deliver the assigned intervention as a supervised exposure to prevent contamination, as a further measure to ensure rigor and transparency. In addition, the study statisticians will be not be blinded in order to manage the dataset, check randomization, check the REDCap™, etc.

## 6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

When the participating pregnant WIC mother is randomly assigned to one of the two study groups through a randomization algorithm conducted through REDCap™, based on her language preference (English vs. Spanish), the subject will be linked to her assigned group and study activities in all time points throughout the duration of the study. In addition, the Data Base Manager and CTRA will keep a separate electronic log and verify any potential compliance issues through monthly data reports created by REDCap™.

Participants will complete pre- and post-intervention questionnaires via REDCap™ at each of the four study visits at the WIC sites. In addition, participants will be sent links with follow-up questionnaires at one and nine months after each visit via texts/emails through REDCap™. Mother's will have up to eight weeks to complete the one- and nine-month questionnaires. REDCap™ will send reminder text messages and emails at one week, two weeks and three weeks for non-responders of the one- and nine-month questionnaires. If mothers do not complete the questionnaires after the first three reminders, REDCap™ will notify the study team, and an RA will contact the mother to complete the questionnaires. Non-responders will also be mailed paper copies of the questionnaires with a prepaid and self-addressed envelope to return once completed.

It is mandatory that study subjects participate in the first visit at the WIC site for enrollment, informed consent and randomization. In addition, in order to participate in all post-intervention activities (i.e., one- and nine-month questionnaires and 3-month booster message), it is mandatory that subjects complete the assigned group intervention activities at the WIC site visit. For example, if a study subject misses a WIC site intervention (visits 1, 2 or 3), they will not complete the post-intervention activities related to the missed visit but will be scheduled for the next WIC site time point intervention.

## 6.5 CONCOMITANT THERAPY

Brief booster messages to help mothers overcome the difficulties of adopting the suggested behaviors will be sent via email and/or text link using REDCap™ at three-month follow-up after they view the videotaped messages at visits 1, 2 and 3. The booster messages for mothers of Group 1 will be autonomous-supportive, while neutral for mothers of Group 2.

### 6.5.1 RESCUE PROCEDURES

Mothers of children diagnosed with caries during the dental exam will be given a list of local dentists to further address their restorative needs. In the course of the children's clinical exams, unexpected conditions might be identified (e.g., dental caries, acute infection, etc.). Should this occur, mothers will be given the following options: 1) to have their children evaluated on the same day on an emergency basis at the UI Department of Pediatric Dentistry, 2) to follow up with their respective local dental providers, or 3) to follow up with the UI Department of Pediatric Dentistry; appointments will be made within 1-4 weeks for further assessment and appropriate treatment. The clinical situation will dictate the urgency of the follow-up care. For example, participants with acute abscess will be strongly encouraged to receive immediate evaluation (e.g., urgent care clinic at UI Department of Pediatric Dentistry or same day visit with their local dentists). Participants with a condition that does not require immediate attention (i.e., asymptomatic dental caries, etc.) could have a longer wait period (e.g. follow up in 4 weeks). In the event that participants decide to follow up with their local dentists, they will be offered the option of a typed document detailing any concerns and oral exam findings. Otherwise, all information collected by the study will be de-identified and not shared with any outside sources.

# 7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

## 7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

This study may be temporarily 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. If the study is prematurely terminated or suspended, the PI will promptly inform study participants of changes to study visit schedule, the IRB and NIDCR, and will provide the reason(s) for suspension or termination.

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

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance of study staff to the protocol (i.e., significant protocol violations)
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility.

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, IRB or other relevant regulatory or oversight bodies.

## 7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

If a participant does withdraw, or is lost to follow up, the Study Termination Case Report Form (CRF) will be completed and entered into REDCap™. The study team will document the reason for participant discontinuation and log the information into an excel file noting that participation is no longer active. Reasons for mothers to be withdrawn from the study or be lost to follow-up may include, but is not limited to mother and/or child moving out of the state, mother losing the child's custody, mother opting to withdraw from study due to having a child born with medical and/or special health care needs conditions that require specialized care and/or hospitalization preventing participation in study activities, etc.

## 7.3 LOST TO FOLLOW-UP

A study WIC mother will be considered lost to follow-up if she is unable to be contacted by the study team to schedule and participate in their WIC site visit activities at year 2, 3 or 4. If participants miss WIC site visits 2 and/or 3, they can still return to the consecutive WIC site visit(s) but will not complete the post-intervention activities (1- and 9-month follow-ups and 3-month booster message) related to missed WIC site visit(s). The study will not replace lost or withdrawn participants.

The following actions must be taken if a participant fails to return to any of the WIC site visits:

- The study team will attempt to contact the participant, reschedule the missed visit within two months, counsel the participant on the importance of maintaining the assigned visit

schedule and ascertain if the participant wishes to and/or should continue in the study; and

- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, three text messages, emails and telephone calls and, if necessary, a letter to the participant's last known mailing address). These contact attempts will be documented in the participant's study file.

Should the participant continue to be unreachable, she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

# 8 STUDY ASSESSMENTS AND PROCEDURES

## 8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

*Endpoints*

- The primary outcome of interest is caries status, which will be measured by the $d_1d_{2-3}$mfscaries criteria for scoring dental caries for the children[44,45-49] Both $d_1$mfs and $d_{2-3}$mfs scores derived from these criteria will be considered, reflecting numbers of affected (cavitated, missing due to caries or filled) surfaces with and without inclusion of non-cavitated ($d_1$ "white spot") lesions. These caries outcomes will be assessed by dental examinations at 12, 24 and 36 months of age. Secondary outcomes of interest will assess changes in maternal knowledge and oral health behaviors through questionnaires via REDCap™, as well as children's plaque and microbial outcomes through dental exams and plaque collection done by dental providers who will be blinded to study allocation.

*Screening and Enrollment*

- The PI and CTRA are responsible for tracking the screening, enrollment, and the number approached, refusals and reasons for refusal. The UI Institute for Clinical and Translational Science IT specialist along with the Database Manager will provide combined enrollment reports of all the WIC sites to the study team and NIDCR.

*Visit Procedure Completion*

- The study CTRA and RAs are responsible for collecting the data at the WIC sites during visits 1, 2, 3 and 4. Participants will view videos and complete questionnaires on tablets/i-pads through REDCap™. UI dental providers will conduct dental exams and collect plaque samples for all participating children. The REDCap™ system will ensure that once a study participant is randomly assigned to one of the two study groups, based on the participant language preference (English vs. Spanish), the participant will be linked to her assigned group and study activities in all time points throughout the duration of the study. In addition, the REDCap™ will also allow us to do complex and robust multivariate data checks, which will be critical for flagging the study team for potential issues within the data or potential process issues at the study sites. The Database Manager will provide reports of number of visits completed for each WIC sites.

*Retention and Attrition*

- The study PI and CTRA are responsible for tracking the recruitment, retention and attrition status throughout the study. Efforts will be made to assess reasons for dropouts.

*Data Entry Errors*

- The Database Manager is primarily responsible for identifying data entry errors in all WIC Sites. REDCap™ will notify the user during data entry of missing fields flagged as

required by data management, and manual queries may be created and issued by the Data Manager.

*Protocol Deviations/Violations*

- A protocol deviation is any noncompliance with the clinical study protocol or GCP. The noncompliance may be on the part of the subject, the investigator, or study staff. The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern. All protocol deviations and violations must be submitted to the UI IRB per its guidelines.
- The CTRA and RAs will be responsible for tracking any deviations/violations. The Protocol Deviations/Violations Tracking Log will be completed and submitted with the report to the Data and Safety Monitoring Board (DSMB). Protocol violations or deviations that meet the definition of an Unanticipated Problem (UP) will be submitted to NIDCR and the Clinical Research Operations and Management Support (CROMS) contractor (rhoproductsafety@rhoworld.com).

## 8.2 SAFETY ASSESSMENTS

Safety monitoring for this study will focus on parameters that capture risks related to study participation. Therefore, the study will collect adverse events (including serious adverse events) and unanticipated problems (UPs) (Title 45 of the Code of Federal Regulations [CFR] Part 46) All UPs, AEs, and SAEs (as defined below) will be reported, from the time of signed informed consent to participant study completion or termination.

## 8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

### 8.3.1 DEFINITION OF ADVERSE EVENTS

An adverse event (AE) 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.

### 8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

SAE is one that meets one or more of the following criteria:

- Results in death
- Is life-threatening (places the participant 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 study participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

### 8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

#### 8.3.3.1 SEVERITY OF EVENT

Each of the AEs and SAEs will be assessed based on the classification systems considering three factors: severity and expectedness of the event and relatedness to this study. Severity of the event will be determined using the classifications outlined below:

- **Mild** - (e.g., signs or symptoms easily tolerated, are of minor irritant not causing loss of time from normal activities or oral function, and do not require therapy or medical/dental evaluation).
- **Moderat**e - (e.g., a low level of inconvenience or concern, may interfere with daily activities or functioning, improved by simple measures);
- **Severe** - (e.g., interrupt normal daily activities, require systemic drug therapy or treatment, incapacitating in performing oral function).

#### 8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All AEs will have their relationship to study procedures, including the intervention, assessed by an appropriately-trained clinician based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Related** – The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.
- **Not Related** – There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

All AEs and SAEs related to this study will be assessed to determine if a protocol amendment will be needed to prevent future occurrences. Corrective and preventive actions will be initiated and the Program Officer at the NIDCR will be notified of these corrective efforts.

#### 8.3.3.3 EXPECTEDNESS

Expectedness of each event will also be assessed to determine whether it is unexpected (e.g., nature not consistent with the intervention in the protocol, consent form, or other related materials) or expected (event is known to be associated with the provided intervention of this study).

### 8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

Any findings which consist of Adverse Events (AE), Serious Adverse Events (SAE) or Unexpected Problems (UP) will be documented on the appropriate Case Report Forms. All AEs, SAEs, UPs, regardless of severity, will be recorded. Potential untoward or unfavorable medical/dental occurrences that occur in a study participant, including any abnormal sign, symptom, or disease (including but not limited to dental pain, dental infection, trauma or other conditions that require immediate attention) that is temporally associated with the subject's participation in the research study (whether or not considered related to the subject's participation in the research) will be identified by all research team members at completion of each study visit and promptly reported to the PI. The PI will record the report on an adverse occurrence report sheet. The PI will also review all reports to determine whether the event is:

1) unexpected;
2) related or potentially related to research study participation; and/or
3) suggests that the research places subjects or others at a greater risk of harm related to the research than was previously known or recognized.

If these three conditions exist, the occurrence will be considered an UP and will be reported to the IRB on the appropriate form and to the NIDCR per their required timeframes. Unanticipated problems will be reported to the DSMB as part of the DSMB reports.

Through these reviews of AEs and occurrences, the DSMB will consider whether cumulative data indicates the need to change the research design, to modify information presented to participants, or to terminate the project. It is anticipated that the committee may decide that due to minimal risk in this behavioral study, there is not a risk for severe AEs that would require a-priori stopping rules (this decision will be reviewed at least annually by the DSMB). Any action taken to suspend or terminate the project will be reported to the UI IRB, the NIH Office of Sponsored Projects, and the program directors at NIDCR. New, scientific developments outside the study that may impact participant safety or the ethics of the study are considered in making these determinations. In addition, in following up AEs, SAEs, UPs, attempts will be made to obtain as much information as possible about event evolution and outcome. Every effort will be made to follow the subject until resolution of the event.

### 8.3.5 ADVERSE EVENT REPORTING

For all AEs that are deemed expected and/or unrelated to the study, a summary will be submitted to the NIDCR Program Officer with the annual progress report, as well as to the UI IRB at the annual continuing review. Adverse events will also be reported to the DSMB as part of DSMB reports.8.3.6 Serious Adverse Event Reporting
Any AE meeting the specified SAE criteria will be submitted on an SAE form to NIDCR's centralized safety system via Rho Product Safety. This report will 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 (the PI) will complete a SAE Form and submit via fax or email within the following timelines:

- All deaths and immediately life-threatening events, whether related or unrelated, will be recorded on the SAE Form and submitted to Product Safety within 24 hours of site awareness.

- SAEs other than death and immediately life-threatening events, regardless of relationship, will be reported within 10 days of site awareness.

All SAEs will be followed until resolution or stabilization.
In addition to being reported to NIDCR, all SAEe will be reported to the UI IRB within 10 business day of the investigator becoming aware of the event. The investigator will submit a Reportable Event form in the electronic IRB submission system at the UI.

### 8.3.7 REPORTING EVENTS TO PARTICIPANTS

If the study is prematurely terminated or suspended, study participants will receive written notification documenting the reason for the study changes.

### 8.3.8 EVENTS OF SPECIAL INTEREST

NA

### 8.3.9 REPORTING OF PREGNANCY

NA

## 8.4 UNANTICIPATED PROBLEMS

### 8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

The Office for Human Research Protections (OHRP) considers UPs involving risks to study participants 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 participant 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 participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

### 8.4.2 UNANTICIPATED PROBLEMS REPORTING

Incidents or events that meet the OHRP criteria for UPs require the creation and completion of an UP report form. We will include the following information when reporting an UP, or any other incident, experience, or outcome to the IRB:

- appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
- a detailed description of the AE, incident, experience, or outcome;
- an explanation of the basis for determining that the AE, incident, experience, or outcome represents an UP;

- a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

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

- UPs will be reported to the IRB within 10 business days of the investigator becoming aware of the event. The investigator will submit a Reportable New Information form in the UI (HAWK-IRB) electronic IRB submission system.
- All UPs 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 UPs will be reported to NIDCR concurrently with reporting to the IRB. These reports will be made to NIDCR's centralized reporting system via Rho Product Safety:

- 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 UP 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

### 8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

If any unanticipated problems occur that may affect the participant's decision to continue participation in the study, study participants will be notified. Safety monitoring for this study will focus on parameters that capture risks related to study participation. The study will collect UPs, including UPs that are also AEs and SAEs (Title 45 of the Code of Federal Regulations [CFR] Part 46). If the study is prematurely terminated or suspended, study participants will receive written notification documenting the reason for the study changes.

# 9 STATISTICAL CONSIDERATIONS

## 9.1 STATISTICAL HYPOTHESES

- Primary Efficacy Endpoint(s):
  - Lower caries incidence

- Secondary Efficacy Endpoint(s):
  - Better knowledge, behavior towards the child's oral health, and levels of salivary MS and visible plaque scores

## 9.2 SAMPLE SIZE DETERMINATION

Based on a sample size of 317, we should be able to entertain up to 31 covariates in a multiple regression model without jeopardizing model validity through overfitting (we note that this far exceeds the number of covariates targeted in this application, even allowing for reasonable examination of first-order interactions); this number would be smaller for logistic modeling, depending upon the distribution of the outcome variable. Finally, we note that modeling of outcomes such as clinical status and behavioral change can include covariates such as knowledge, behavioral intent, autonomy, competence, and relatedness. Such models incorporate the key aspects of the SDT intervention, can assist in the evaluation of the impact of SDT, and can offer validation of its application. The rich data set will permit formal evaluation of the validity of the theoretical basis of the proposed intervention, e.g., by evaluation of timing of behavioral change and whether it persists as prescribed by SDT, by assessing the relationships between outcomes and ratings of autonomy, competence and relatedness, and more systematically by use of mediation models.[58-62] While every effort will be made to maximize retention as outlined below, missing data issues will be addressed via multiple imputation[63,64] the importance and utility of this approach have been substantiated for intervention trials targeting early childhood caries.[65] We will follow the general recommendations of Rubin[66,67] and emulate the more specific aspects of execution of the caries-oriented analysis applied to these reported caries intervention trial data.[65] The possibility of selective dropout between the two groups will be fully explored, as will characteristics associated with dropout; sensitivity analyses will be conducted to explore the potential impact on results.

*Power and Sample Size Considerations: Estimation of Detectable Effect Sizes*

For purposes of sample size calculation, the primary outcomes of interest are caries status as measured by the $d_1$-$_{2\text{-}3}$mfs and $d_{2\text{-}3}$mfs indices at the third-year follow-up, i.e., at approximately three years of age; caries status at two-year follow-up represents a secondary outcome. Indices are derived from the modified $d_1d_{2\text{-}3}$mfs caries criteria. Required sample sizes are primarily based upon the experiences reported by Wagner et al,[68] which were felt to provide the most appropriate estimates of effect sizes and variability after translation from the WHO caries criteria. Therefore, assuming an effect size (treatment difference) of 1.1 (standard deviation 3.45) for the number of cavitated, missing or filled lesions, Type I error level of 0.05, and 80% power, required sample size is 156 children per group at the three-year follow-up. Given enrollment of 317 mother-child dyads for each group (experimental (SDT) video or neutral control), and a conservative annual attrition rate of 21%, 156 dyads per group (312 total) would be expected to

complete three-year follow-up. Based upon these sample sizes, we would have 93% power to detect a treatment difference of 1.7 (given s.d. of 4.35) if the caries index also included white spot lesions, based on the observations of Wagner et al.[68] As described in the previous section, somewhat more optimistic retention rates may be realistically anticipated: if we assume an attrition schedule of 21% the first year and 15% for each of the two subsequent years, we would anticipate that initial recruitment of 317 dyads per group would result in about 180 dyads per group completing 3-year follow-up, corresponding to 85% power to detect a 1.1 difference in $d_{2-3}$mfs and 95% power to detect a 1.7% difference in $d_1d_{2-3}$mfs. Sensitivity analyses drew upon available data on children aged 26-30 months from our WIC-based studies in three Eastern Iowa Cities[10,11,50-52,69] and the literature. Our studies[10-13,49-54] suggest the standard deviation of both of these indices is slightly less than 3.0 surfaces, which would be expected to result in slightly higher power estimates that those given above; however, we will be drawing from a wider geographic area of the state, and somewhat greater variability has been reported for other WIC populations.[70,71] We note that we have adequate power to detect smaller effect sizes than were noted at two years in the intervention trial of Harrison et al[72] comparing the effect of motivational interviewing and control on ECC; moreover, they are similar to, or less than, the observed but non-significant differences for caries outcomes in a smaller study among First Nations children that also compared the effects of MI counseling vs. control.[73] They will also provide some protection against loss of power should response rates be less than projected or in the case of misspecification of the statistical assumptions.

## 9.3 POPULATIONS FOR ANALYSES

Our primary population for analyses will be the intention-to-treat population. For a sensitivity analysis, the per-protocol population will also be considered. The per-protocol dataset includes subjects who complete the three visits and answer ‘yes’ to watching all booster messages.

## 9.4 STATISTICAL ANALYSES

### 9.4.1 GENERAL APPROACH

**Randomization**

A block-level randomization scheme with a 1:1 allocation ratio will be used to determine interventions for individuals. Random block sizes of 2, 4, and 6 will be used to create the randomization scheme. Randomization will be stratified on primary language and site to ensure balance between the intervention groups. There will be 12 possible sites in the study.

### 9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

**Primary efficacy**

The primary outcome is caries status, measured by the $d_1d_{2-3}$ caries criteria for scoring dental caries in children developed by members of the Iowa Fluoride Study. Caries status as total counts of dmf surfaces will be calculated during yearly dental exams. These counts will be reported as means, medians, quartiles, standard deviations, and ranges for each intervention group. Data will be explored longitudinally using dmf surfaces at each age and dmf increments between ages. Analysis of caries outcomes will focus on Poisson and/or negative binomial modeling, possibly with variance inflation and zero inflation accommodation, as appropriate. To account for repeated longitudinal measurements, generalized estimating equations (GEEs) will be used to model these counts. A first-order autoregressive or AR(1) working correlation structure will be

assumed. The quasi-likelihood information criteria (QIC) will be used to compare models to select the best fit. The model will include age, gender, location (urban/rural), race, intervention, and mothers' knowledge and behavior. These are all clinically important known covariates that are associated with caries status, and mothers' intervention and behavior/knowledge are covariates of interest. These are planned covariates to include; however, if the number of covariates is limited by the sample size or infrequent observations of caries, we will use bivariate analyses to inform a more parsimonious final model. Results for the model will be presented as incidence rate ratios with 95% confidence intervals. Data will be analyzed on an intention-to-treat basis with sensitivity analyses considering the per-protocol dataset. Missing data will be addressed via multiple imputation and sensitivity analyses will be conducted to explore potential impacts on results.

### 9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

**Secondary efficacy**

Secondary outcomes of interest include changes in knowledge and oral health behaviors of mothers, as well as plaque and microbial outcomes in children. Knowledge outcomes will be measured pre and post intervention via the score on the knowledge assessment. These measures will be considered as counts. GEE modeling will be used with Poisson or negative binomial distributions considered. Results will be presented as incidence rate ratios and 95% confidence intervals.

Maternal change in behavior will be assessed via a set of behavioral questions asked at multiple time points. Each individual question will be dichotomized into improved vs. did not improve based on the answers given pre and post intervention. When analyzing single time points, logistic modeling will be used. To evaluate behavioral changes over time, GEE models with a logit link function will be used. Results will be presented as odds ratios and 95% confidence intervals.

Visible plaque will be analyzed as the number of maxillary and mandibular incisors and molars with plaque at each visit. Analysis of plaque outcomes will focus on Poisson and/or negative binomial modeling, possibly with variance inflation and zero inflation accommodation, as appropriate. To account for repeated longitudinal measurements, GEE will be used to model these counts. Results will be presented as incidence rate ratios and 95% confidence intervals.

Levels of salivary MS will be reported as numbers of bacteria from each visit. Log transformation will be considered if data is skewed, and GEE models assuming a normal distribution with an identity link will be used when analyzing multiple time points. Results will be presented as adjusted least squares means estimates and 95% confidence intervals.

The same covariates as the primary endpoint will be used for both bivariate and multivariable modeling, subject to the constraint of 10 observations/events for every covariate included. Missing data may be addressed via multiple imputation. An AR(1) correlation structure will be assumed for all longitudinal models. QIC will be used for all model/covariate selection involving GEEs; AIC will be used for models calculated for single time points. Mediation analyses will proceed via Baron and Kenny's[74] steps for mediation analysis and significance will be calculated via Sobel tests.

### 9.4.4 SAFETY ANALYSES

NA

### 9.4.5 BASELINE DESCRIPTIVE STATISTICS

**Baseline descriptive analysis**

For continuous demographic variables, the mean, median, and range will be calculated for each group (intervention and control). For categorical demographic variables, the frequency and percent of each category will be calculated for each group.

### 9.4.6 PLANNED INTERIM ANALYSES

**Planned interim analysis**

No interim analyses are planned.

### 9.4.7 SUB-GROUP ANALYSES

To determine whether the effect of the assigned intervention is consistent across subgroups, similar models for both primary and secondary endpoints will be fit and estimated including but not limited to the following:

- Mother education level
- First time mother or not
- Mother income
- Mother race
- Mother oral health status
- Mother age (< 25 vs. 25 or older)

No subgroup analysis by sex will be performed, as only pregnant individuals will be enrolled in the study.

### 9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

**Tabulation of individual participant data**

Data will be de-identified and presented anonymously.

### 9.4.9 EXPLORATORY ANALYSES

**Exploratory analysis**

NA

# 10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

## 10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

### 10.1.1 INFORMED CONSENT PROCESS

#### 10.1.1.1 CONSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Prior to the beginning of the study, the PI must have IRB approval for the protocol and any informed consent forms. Any other information provided to the participants must have IRB approval. Only the PI or research team members approved by the IRB may administer consent. A person is qualified to administer consent only if he/she has received basic human subject's protection training and possesses the requisite dental and/or medical training, knowledge of the protocol and familiarity with the clinical needs to be able to discuss the risks and benefits of the study with prospective participants.

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. Consent in this study will be sought from all WIC-enrolled pregnant women interested in participating in the study. The consent of each pregnant woman will be obtained in a quiet private space by a trained research member. The consent form will be reviewed verbally. Throughout the consent process, the research member will ask the pregnant woman if she has any questions. The staff member will make sure the individual has adequate time to consider all options. If the individual appears to need more time to consider all options, staff will provide the option to participate at a later time. All pregnant women will be given the study staff's contact information in case they decide to join the study. Informed consent will be administered electronically via REDCap™ web-based research software.

The participant will be asked to sign the informed consent form electronically in REDCap™ prior to any study-related assessments or procedures. All participants will be given a copy of the signed form, either by email or printed on site directly following consent. Back up paper copies of all consent forms will be on hand in case of any power outages or Wi-Fi connectivity issues. Due to the child participants' age, informed consent will be obtained from the mother of the future child participant.

#### 10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Documentation of Consent – The ICH GCP guidelines require that the participant or legal representative receive a copy of the signed and dated consent document. In this study the study participants will be asked to sign and date the informed consent document electronically and will be provided with a signed and dated copy by email or a printed copy. The source documents will thus reside in REDCap™ and will indicate that the consent was signed, along with the date of signing.

Translation of Consent Documents – All participants need to be able to speak and read English or Spanish. Therefore, all materials, including consents, will be translated and made available in English and Spanish.

### 10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be 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. If the study is prematurely terminated, the PI will promptly inform study participants, the IRB and NIDCR, and will provide the reason(s) for suspension or termination.

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

- Determination of unexpected, significant, or unacceptable risk to participants.
- Demonstration of efficacy that would warrant stopping.
- Insufficient compliance of study staff to the protocol (i.e., significant protocol violations).
- Data that are not sufficiently complete and/or evaluable.
- Determination that the primary endpoint has been met.
- Determination of futility.

### 10.1.3 CONFIDENTIALITY AND PRIVACY

Our research team will maintain rigorous protocols to ensure that data remain confidential. These methods include training of all research team members on issues of confidentiality and ethical research conduct, breaking the links between contact information and individual identifiers in the participant data, the use of secure passwords for access to data, and the use of secure filing cabinets. All researchers and staff will be required to keep all information collected by this project confidential. A REDCap™ program at the UI will maintain the list linking each participant with a unique identifier. This list will be maintained in a physically separate location from the research database(s) with the unique identifier. The PI will have ultimate responsibility for managing and maintaining the data.

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency.

All research activities will be conducted in as private a setting as possible.

A study monitor, other authorized representatives of the IRB, may inspect all documents and records required to be maintained by the investigator, including but not limited to, records for the participants in this study.

The study participant's contact information will be securely stored for internal use only during the study. At the end of the study, all records will continue to be kept in a secure location for as

long a period as dictated by the reviewing UI IRB, Institutional policies, or sponsor/funding agency requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the Institute for Clinical and Translational Services (ICTS) at the UI using REDCap™. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study data management system used by our research team will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at ICTS.

### 10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Stored specimens will be used for future studies. The participating child's samples will be stored with a code which may be linked to the child's name. If the mother agrees during the informed consent for future use of her child's samples but decide in the future that she would like to have it removed from future research, she should contact the PI. However, if some research with the child's samples had already been completed, the information from that research may still be used.

All paper-based data at the UI will be stored in the PI's locked private office within locked filing cabinets, including external hard drives with back up study data. Electronic data will be stored on the password-protected web-based REDCap™ site. No study data will remain on laptops after data collection visits end. All specimen and data will be stored for a minimum of six years upon study completion as dictated by the UI IRB.

Subjects may refuse or withdraw consent for collected samples and data to be used for future studies as described in the consent form. IRB will review future studies, and protections of confidentiality for any future studies with the stored specimens and/or data.

### 10.1.5 KEY ROLES AND STUDY GOVERNANCE

| Role | Responsibilities |
|---|---|
| **Principal Investigator**<br>Karin Weber-Gasparoni, DDS, MS, PhD<br>Professor and Chair<br>Infant Oral Health Program Director<br>Department of Pediatric Dentistry<br>University of Iowa College of Dentistry<br>S202 Dental Science South<br>Iowa City, IA 52242<br>Office phone: (319) 335-7486<br>Office fax: (319) 353-5508<br>karin-weber@uiowa.edu | • Study leadership<br>• Study design<br>• General study issues<br>• Protocol questions<br>• Reporting adverse events<br>• Data analysis<br>• Results interpretation<br>• Dissemination of findings<br>• Gold standard for calibration trainings<br>• Write abstracts, presentations<br>• Prepare manuscripts for publication |
| **Program Official**<br>Dr. Elise Rice | • Normal stewardship of the award<br>• Provide scientific, programmatic, and technical aspects of this project |

| | |
|---|---|
| NIH NIDCR<br>6701 Democracy Boulevard<br>MSC 4878<br>Bethesda, MD 20892<br>United States<br>(301) 594-4814<br>elise.rice@nih.gov | |
| **Project Scientist**<br>Dr. Melissa Riddle<br>NIH NIDCR<br>6701 Democracy Blvd<br>MSC 4878<br>Bethesda, MD 20892-4878<br>United States<br>(301) 451-3888<br>riddleme@nidcr.nih.gov | • Provide technical assistance, advice, and coordination above and beyond normal program stewardship for grants<br>• Responsible for assessing the progress of the project toward the accomplishment of the goals and for recommending if further funds should be released to the project<br>• Facilitate the establishment of contacts and collaborations between awardees and other persons or organizations whose participation will assist with the accomplishment of project goals |
| **NIDCR Medical Monitor**<br>Dr. Kevin McBryde<br>National Institutes of Health (NIH)<br>BG 1DEM RM 638<br>6707 Democracy Blvd<br>Bethesda, MD 20817<br>Phone: (301) 594-0170<br>Fax: (301) 480-8319<br>kevin.mcbryde@nih.gov | |
| **Co-Investigators**<br>• David Drake, PhD<br>david-drake@uiowa.edu<br>(319)-335-7384<br>• Steven Levy, DDS, MPH<br>steven-levy@uiowa.edu<br>(319)-335-7185<br>• Teresa Marshall, PhD<br>teresa-marshall@uiowa.edu<br>(319)-335-7190<br>• John Warren, DDS, MS<br>john-warren@uiowa.edu<br>(319)-335-7205<br>• Xian Jin Xie, PhD<br>xianjin-xie@uiowa.edu<br>(319)-335-7214 | • Advise on study design and operation<br>• Aid in study protocols and instruments<br>• Implement recruitment/retention strategies<br>• Conduct dental exam calibration training<br>• Data management, analysis, and interpretation<br>• Write abstracts, poster presentations<br>• Prepare manuscripts for publication |

| | |
|---|---|
| **Clinical Trials Research Associate**<br>• Jennifer Bowman-Reif, MS<br>jennifer-bowman-reif@uiowa.edu<br>(319)-467-4930<br><br>**Research Assistants**<br>• Garrett Ormsby, BS<br>garrett-ormsby@uiowa.edu<br>(319)-467-4930<br>• Ethan Heusel, BA<br>ethan-heusel@uiowa.edu<br>(319)-467-4930<br>• Erin Striegel, BS<br>erin-striegel@uiowa.edu<br>(319)-467-4930 | • Project support & administration<br><br>• Participant recruitment, enrollment, scheduling, and reminders<br>• Data collection & management<br>• Main contact and resource for participants<br>• Resource to participants to answer questions and resolve problems for study subjects |
| **Consultants**<br><br>*University of California, San Francisco*<br>• Stuart Gansky, DrPH<br>stuart.gansky@ucsf.edu<br>(415)-502-8094<br>*Australian Catholic University*<br>• Johnmarshall Reeve, PhD<br>johnmarshall.reeve@acu.edu.au<br>(612)-9739-2172 | • Assist with dental exam calibration training<br>• Aid in creation of REDCap™ calibration data collection<br>• Aid in study protocols and instruments related to the behavioral intervention (SDT)<br>• Develop and monitor study fidelity<br>• Collaborate with community partners with any study issues/concerns<br>• Data interpretation<br>• Write abstracts, poster presentations<br>• Prepare manuscripts for publication |
| **Dental examiners**<br>• Amy Lesch, DDS, MS<br>amy-lesch@uiowa.edu<br>(319)-467-1464<br>• Dental Hygienists (n=2) TBD<br>• Principal investigator | • Examine children for caries<br>• Obtain plaques samples |
| **Data & Statistics Team**<br>• Xian Jin Xie, PhD<br>xianjin-xie@uiowa.edu<br>(319)-335-7214<br>• Erliang Zeng, PhD<br>erliang-zeng@uiowa.edu<br>(319)-335-7302<br>• Chandler Pendleton, MS<br>chandler-pendleton@uiowa.edu | • Data management and analysis<br>• Monitor data quality<br>• Advise on research design<br>• Data analysis<br>• Address any potential statistical issues<br>• Data base manager: construct the database, edits, and randomization, create reports, provide training on queries and |

| | |
|---|---|
| (319)-467-3166 | report generation, export data, lock the database, and provide study close out materials. |
| **ICTS REDCap™ Senior IT Support**<br>• Joseph Spring, BS<br>joseph-spring@uiowa.edu<br>(319)-353-6299 | • Design and implementation of custom instruments in REDCap™<br>• Development of Alerts and Notifications to support the study<br>• Development automation for sending of follow-up surveys based on timing of logic<br>• Creating reports within REDCap™ for study team<br>• Twilio<br>• Multi language module<br>• Randomization (variable number of sites) |
| **Laboratory Manager**<br>• David Drake, PhD<br>david-drake@uiowa.edu<br>(319)-335-7384<br><br>Min Zhu<br>Min-zhu@uiowa.edu<br>(319) 335-6986 | • Plaque sample preparation<br>• Processing of biomarker data<br>• Lab safety, chemical inventory, and hazardous waste disposal<br>• Record and interpret microbiological data<br>• Responsible for salivary bacterial analysis |
| **WIC Clinic Staff**<br>• Cedar Rapids (3 sites)<br>• Davenport (2 sites)<br>• Muscatine (1 site)<br>• Washington (1 site)<br>• Clinton (1 site)<br>• Dewitt (1 site)<br>• Waterloo (1 site)<br>• Dubuque (1 site)<br>• Makoqueta (1 site)<br>• Johnson (1)<br>• UIHC (1) | • Participant recruitment – WIC study staff will provide informational brochure to pregnant WIC clients interested in hearing about the study<br>• WIC clinics will serve as study sites |

### 10.1.6 SAFETY OVERSIGHT

The PI will be responsible for study oversight, including monitoring safety, ensuring that the study is conducted according to the protocol and ensuring data integrity. The interventions, outcome measures, and other assessments are of minimal risk to participants in the proposed study. Intervention participation and data assessments do not exceed the probability and magnitude of harm or discomfort anticipated during ordinarily encountered daily life or in the performance of routine oral or psychological examinations or tests. The PI will oversee

recruitment and consenting processes approved for participants and conduct the study using protocols that will be approved by the UI IRB. Systems will be in place to assure confidentiality and data security for data collection and storage. The PI and the CTRA will review the data for safety concerns and data trends at regular intervals and will promptly report to the IRB and NIDCR per their reporting requirements.

In addition to the PI's responsibility for oversight, study oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) composed of members with expertise in obstetrics/gynecology, motivational interviewing and health disparities, pediatric dentistry, and biostatistics. Reports will be provided to the DSMB, including missing data, protocol deviations and safety data, screen fail, enrollment and withdrawal rates, etc. 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.

### 10.1.7 CLINICAL 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 NIDCR's CROMS contractor. The monitor will evaluate study processes and documentation based on NIDCR standards and the ICH GCP.

Details of clinical site monitoring will be documented in a Clinical Monitoring Plan (CMP) developed by the CROMS contractor, in collaboration with the NIDCR Office of Clinical Trials and Operations Management (OCTOM) and the NIDCR Program Official. The CMP will specify the frequency of monitoring, monitoring procedures, the level of clinical site monitoring activities (e.g., the percentage of subject 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 the CROMS contractor 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, OCTOM, and the NIDCR. The NIDCR reserves the right to conduct independent audits as necessary.

#### PREPARING FOR AUDITS BY REGULATORY AUTHORITIES

The NIDCR reserves the right to conduct independent audits as necessary. Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

### 10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

All clinical site level quality management efforts will be supervised by the PI, aided by the CTRA and with input from the co-investigators. Details of the quality processes will be included

in the quality management plan. Research team 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.

### 10.1.9 DATA HANDLING AND RECORD KEEPING

#### 10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection will be the responsibility of the clinical trial staff at the site under the supervision of the PI and CTRA. The PI will be responsible for ensuring the accuracy, completeness, and timeliness of the data reported. UPs must be reviewed by the PI. The research team will be trained on electronic data collection, particularly with regard to upholding the study intervention fidelity. In addition, proper training will be conducted among clinical examiners who will perform the dental exams and plaque collections, as well as among those involved in the storage and transport of plaque samples.

The PI and co-investigators will be responsible for ensuring data integrity. Data management will be handled at the UI College of Dentistry by a dedicated database manager, who will construct the database, provide data entry training, create reports, and be responsible for data quality and management procedures, data edits, queries and report generation, exporting the data, locking the database, and providing study close out materials. The database will be established using REDCap™ (Research Electronic Data Capture), a reliable and secure web-based application developed at Vanderbilt University and supported by the UI.

#### 10.1.9.2 STUDY RECORDS RETENTION

Study records will be maintained for at least six years, to comply with institutional policy, from the date that the grant federal financial report is submitted to the NIH or from the date of the final publication, whichever is later.

### LONG TERM STORAGE OF FORMS

All final, cleaned data in REDCap™ will be exported to a CSV file and saved on the UI server. The REDCap™ database will be closed and archived and all user rights withdrawn. Data will be retained for at least 6 years from the end of the study.

### 10.1.10 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical study protocol or GCP. The noncompliance may be on the part of the subject, the investigator, or study staff. The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern. In addition, the study will notify the UI IRB and NIDCR, per their reporting requirements.

### 10.1.11 PUBLICATION AND DATA SHARING POLICY

The study will comply with NIH Public Access Policy, which ensures that the public has access to the published results of NIH-funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central within 12 months upon publication. The research team will be responsible for developing

publication procedures and resolving authorship issues. Manuscripts will be reviewed by all the co-authors before submission. Data will be shared no later than the acceptance for publication of the main findings from the final data set.

### 10.1.12 CONFLICT OF INTEREST POLICY

All study investigators will file conflict of interest and financial disclosure forms with the UI as needed or requested.

## 10.2 ADDITIONAL CONSIDERATIONS

N/A

## 10.3 ABBREVIATIONS AND SPECIAL TERMS

| | |
|---|---|
| AE | Adverse Event |
| AR | First-order autoregressive |
| CFR | Code of Federal Regulations |
| CMP | Clinical Monitoring Plan |
| CRF | Case Report Form |
| CROMS | Clinical Research Operations and Management Support |
| CSV | Comma-separated values |
| CTRA | Clinical Trial Research Associate |
| dmf | Decayed, Missing, and Filled Tooth |
| DSMB | Data Safety Monitoring Board |
| ECC | Early childhood caries |
| GCP | Good Clinical Practice |
| GEE | Generalized estimating equation |
| HCCQ | Health care climate questionnaire |
| HIPAA | Health Insurance Portability and Accountability Act |
| ICH | International Conference on Harmonisation |
| ICTS | Institute for Clinical and Translational Services |
| IRB | Institutional Review Board |
| MS | mutans streptococci |
| NIDCR | National Institute of Dental and Craniofacial Research |
| NIH | National Institutes of Health |
| OCTOM | Office of Clinical Trials and Operations Management |
| OHRP | Office for Human Research Protections |
| PI | Principal Investigator |
| QA | Quality Assurance |
| QC | Quality Control |
| REDCap™ | Research Electronic Data Capture |
| SAE | Serious Adverse Event |
| SDT | Self-determination theory |

| | |
|---|---|
| SOA | Schedule of Activities |
| UI | University of Iowa |
| UP | Unanticipated Problem |
| US | United States |
| WIC | Women, Infants and Children |
| WHO | World Health Organization |

## 10.4 PROTOCOL AMENDMENT HISTORY

| Version | Date | Description of Change | Brief Rationale |
|---|---|---|---|
| | | | |

## 11 REFERENCES

1. Onken LS, Carroll KM, Shoham V, Cuthbert BN, Riddle M. Reenvisioning clinical science: Unifying the discipline to improve public health. Clin Psychol. 2014;2(1):22-34.
2. Virtanen JI, Vehkalahti KI, Vehkalahti MM. Oral health behaviors and bacterial transmission from mother to child: an explorative study. BMC Oral Health. 2015;(3):15-75.
3. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. Am Psychol. 2000;55(1):68-78.
4. Johnmarshall Reeve & Sung Hyeon Cheon. Autonomy-supportive teaching: Its malleability, benefits, and potential to improve educational practice, Educational Psychologist. 2021;(56:1):54-77
5. Dye BA, Li X, Lewis BG, Iafolla T, Beltran-Aguilar ED, Eke PI. Overview and quality assurance for the oral health component of the National Health and Nutrition Examination Survey (NHANES), 2009-2010. J Public Health Dent. 2014;74(3):248-56.
6. Marshall TA, Levy SM, Broffitt B, Warren JJ, Eichenberger-Gilmore JM, Burns TL, Stumbo PJ. Dental caries and beverage consumption in young children. Pediatrics. 2003;112(3):184-91.
7. Kolker JL, Yuan Y, Burt BA, Sandretto AM, Sohn W, Lang SW, Ismail AI. Dental caries and dietary patterns in low-income African American children. Pediatr Dent. 2007;29(6):457-64.
8. Alaluusua S, Malmivirta R. Early plaque accumulation – a sign for caries in young children. Community Dentistry & Oral Epidemiology. 1994;22:273-76.
9. Kanellis, M.J. Caries risk assessment and prevention: strategies for Head Start, Early Head Start and W.I.C. J Pub Health Dent 2000;60:210-17.
10. Warren JJ, Weber-Gasparoni K, Marshall TA, Drake DR, Dehkordi-Vakil F, Kolker JL, Dawson DV. Factors associated with dental caries experience in 1-year-old children. J Public Health Dent. 2008;68(2):70-5.
11. Warren JJ, Weber-Gasparoni K, Marshall TA, Drake DR, Dehkordi-Vakil F, Dawson DV, Tharp KM. A longitudinal study of dental caries risk among very young low SES children. Community Dent Oral Epidemiol. 2009;37(2):116-22.
12. Nair R, Weber-Gasparoni K, Levy SM, Warren JJ, Marshall TA, Qian F. Factors affecting early childhood caries among WIC enrolled children in Linn County, Iowa. J Dent Child. 2010;77(3):158-65.
13. Weber-Gasparoni K, Goebel BM, Warren JJ, Drake DR, Reeve J, Kramer KWO, Dawson DV. Factors associated with Mutans Streptococci among young WIC-enrolled children. J Public Health Dent. 2012;72(4):269-78.
14. Berkowitz RJ, Turner J, Hughes C. Microbial characteristics of the human dental caries associated with prolonged bottle feeding. Archives of Oral Biology. 1984;29:949-51.
15. Caufield PW. Dental caries – a transmissible and infectious disease revisited: a position paper. Journal of Pediatric Dentistry 1997;19(8):491-98.
16. Berkowitz RJ Mutans streptococci: acquisition and transmission. Pediatr Dent. 2006;28(2):106-9.
17. Wan AKL, Seow WK, Purdie DM, Bird PS, Walsh LJ, Tudehope DI. Oral colonization of Streptococcus mutans in six-month-old predentate infants. J Dent Res. 2001;80(12):2060-5.
18. O'Sullivan DM, Douglass JM, Champany R, Eberling S, Tetrev S, Tinanoff N. Dental caries prevalence and treatment among Navajo preschool children. Journal of Public Health Dentistry. 1994;54:139-44.

19. Dye BA, Afful J, Thornton-Evans G, Iafolla T. Overview and quality assurance for the oral health component of the National Health and Nutrition Examination Survey (NHANES), 2011-2014. BMC Oral Health. 2019;19(1):95.
20. Kovarik R, Skelton J, Mullins R, Langston L, Womack S, Morris J, Martin D, Brooks R, Ebersole JL. CenteringPregnancy Smiles: A community engagement to develop and implement a new oral health and prenatal care model in rural Kentucky. J Higher Educ Outreach and Engagement. 2009:13(3):101-11.
21. Alsada LH, Sigal MJ, Limeback H, Fiege J, Kulkarni GV. Development and testing of an audio-visual aid for improving infant oral health through primary caregiver education. J Can Dent Assoc. 2005;71(4):241, 241a-241h.
22. Ng JYY, Ntoumanis N, Thogersen-Ntoumani C, Deci EL, Ryan RM, Duda JL, Williams GC. Self-determination theory applied to health contexts. Perspectives on Psychological Science. 2012;7:325-40.
23. Ryan RM, Deci EL. (2017). Self-determination theory; Basic psychological needs in motivation, development, and wellness. New York, NY: Guilford Press.
24. Williams GC, McGregor HA, Zeldman A, Freedman ZR, Deci EL. Testing a self-determination theory process model for promoting glycemic control through diabetes self-management. Health Psychol. 2004;23(1):58-66.
25. Ryan RM, Deci EL. Self-regulation and the problem of human autonomy: Does psychology need choice, self-determination, and will? Journal of Personality. 2006;74:1557-86.
26. Vansteenkiste, Maarten, Ryan, R., & Deci, E. (2008). Self-determination theory and the explanatory role of psychological needs in human well-being. In L. Bruni, F. Comim, & M. Pugno (Eds.), Capabilities and happiness (pp. 187–223). Oxford;United Kingdom: Oxford University Press.
27. Williams GC, Grow VM, Freedman Z, Ryan RM, Deci EL. Motivational predictors of weight loss and weight-loss maintance. J Pers Soc Psychol. 1996;70:115-26.
28. Reeve J, Cheon SH. (2014) An intervention-based program of research on teachers' motivating styles. In S. Karabenick, T. Urdan's (Eds.), Advances in motivation and achievement: Motivational interventions (Vol. 18, pp. 293-339). Bingley, England: Emerald Group.
29. Cheon SH, Reeve J, Song YG. A teacher-focused intervention to decrease PE students' amotivation by increasing need satisfaction and decreasing need frustration. Journal of Sport and Exercise Psychology. 2016;38:217-35.
30. Cheon SH, Reeve J, Yu TH, Jang HR. The teacher benefits from giving autonomy support during physical education instruction. Journal of Sport and Exercise Psychology. 2014;36:331-46.
31. Cheon, S. H., Reeve, J., Lee, Y., Ntoumanis, N., Gillet, N., Kim, B. R., & Song, Y. G. Expanding autonomy psychological need states from two (satisfaction, frustration) to three (dissatisfaction): A classroom-based intervention study. Journal of Educational Psychology. 2019;111(4), 685.
32. Ryan, R. M., Deci, E. L., Vansteenkiste, M., & Soenens, B. A legacy unfinished: An appreciative reply to comments on self-determination theory's frontiers and challenges. Motivation Science. 2021;7(2), 120.
33. Silva MN, Markland D, Carraça EV, Vieira PN, Coutinho SR, Minderico CS, Matos MG, Sardinha LB, Teixeira PJ. Exercise autonomous motivation predicts 3-yr weight loss in women. Med Sci Sports Exerc. 2011;43(4):728-37.

34. Williams GC, Rodin GC, Ryan RM, Grolnick WS, Deci EL. Autonomous regulation and long-term medication adherence in adult outpatients. Health Psychol. 1998;17(3):269-76.
35. Williams GC, Patrick H, Niemiec CP, Williams LK, Divine G, Lafata JE, Heisler M, Tunceli K, Pladevall M. Reducing the health risks of diabetes: how self-determination theory may help improve medication adherence and quality of life. Diabetes Educ. 2009;35(3):484-92.
36. Williams GC, McGregor H, Sharp D, Levesque CS, Kouides RW, Ryan RM, Deci EL. Testing a self-determination theory intervention for motivating tobacco cessation: Supporting autonomy and competence in a clinical trial. Health Psychol 2006;25:91-101.
37. Williams GC, Niemiec CP, Patrick H, Ryan RM, Deci EL. The importance of supporting autonomy and perceived competence in facilitating long-term tobacco abstinence. Ann Behav Med. 2009;37(3):315-24.
38. Halvari AE, Halvari H. Motivational predictors of change in oral health: An Experimental test of self-determination theory. Motiv Emot. 2006;30:294-305.
39. Halvari AEM, Halvari H, Bjørnebekk G, Deci EL. Self-determined motivational predictors of increases in dental behaviors, decreases in dental plaque, and improvement in oral health: a randomized clinical trial. Health Psychol. 2012;31(6):777-88.
40. Halvari AEM, Halvari H, Bjørnebekk G, Deci EL. Motivation and anxiety for dental treatment: Testing a self-determination theory model of oral self-care behavior and dental clinic attendance. Motiv Emot 2010;34:15-33.
41. Halvari AEM, Halvari H, Bjørnebekk G, Deci EL. Motivation for dental home care: Testing a self-determination theory model. J Applied Soc Psychol. 2012;42(1):1-39.
42. Beck JD, Lawrence HP, Koch GG. Analytic approaches to longitudinal caries data in adults. Community Dent Oral Epidemiol. 1997;25:42-51.
43. Beck JD, Lawrence HP, Koch GG. A method for adjusting caries increments for reversals due to examiner misclassification. Community Dent Oral Epidemiol. 1995;23:321-30.
44. Warren JJ, Levy SM, Kanellis MJ. Dental caries in the primary dentition: Assessing prevalence of cavitated and noncavitated lesions. Journal of Public Health Dentistry 2002;62(2):109-14.
45. UCSF Glass Ionomer Sealant and Fluoride Varnish Study to Prevent Early Childhood Caries (GIFVT) http://www.clinicaltrials.gov/ct2/show/NCT01129440.
46. UCD Promoting Behavioral Change for Oral Health in American Indian Mothers and Children http://www.clinicaltrials.gov/ct2/show/NCT01116726.
47. UCD Preventing Caries in Preschoolers: Testing a Unique Service Delivery Model in American Indian Head Start Programs http://www.clinicaltrials.gov/ct2/show/NCT01116739.
48. BU Tooth Smart Healthy Start: Oral Health Advocates in Public Housing: http://www.clinicaltrials.gov/ct2/show/NCT01205971.
49. Warren JJ, Weber-Gasparoni K, Tinanoff N, Batliner TS, Jue B, Santo W, Garcia RI, Gansky SA. Early childhood caries collaborating centers. Examination criteria and calibration procedures for prevention trials of the early childhood caries collaborating centers. J Public Health Dent. 2015;75(4):317-26.
50. Weber-Gasparoni K, Kanellis MJ, Ansley T, Reeve J, Drake DR, Craft-Rosenberg M (2003). A comparison of the effectiveness of three educational intervention in the prevention of early childhood caries (Ph.D. Dissertation).

51. Weber-Gasparoni K, Reeve J, Ghosheh N, Warren JJ, Drake DR, Kramer KW, Dawson DV. An effective psychoeducational intervention for early childhood caries prevention: part I. Pediatr Dent.2013;35(3):241-6.
52. Weber-Gasparoni K, Warren JJ, Reeve J, Drake DR, Kramer KW, Marshall TA, Dawson DV. An effective psychoeducational intervention for early childhood caries prevention: part II. Pediatr Dent.2013;35(3):247-51.
53. Shonka JM, Weber-Gasparoni K, Kramer KW, Warren J, Marshall TA, Dawson DV. Spill-proof beverage container usage among young WIC-enrolled children. Pediatr Dent. 2014;36(3):222-7.
54. Saba AH, Warren JJ, Weber-Gasparoni K, Dawson DV. Retention of low income children in three dental studies investigating early childhood caries, Journal of Health Disparities Research and Practice: Vol. 7: Iss. 4, Article 7. Available at: http://digitalscholarship.unlv.edu/jhdrp/vol7/iss4/7.
55. Avasare T, Warren J, Qian F, Marshall T, Weber-Gasparoni K, Drake D. Longitudinal study assessing factors associated with Mutans Streptococci acquisition in infants and toddlers. Oral Health Prev Dent. 2017;15(6):543-48.
56. Prestwich A, Webb TL, Conner M. Using theory to develop and test interventions to promote changes in health behaviour: Evidence, issues, and recommendations. Current Opinion in Psychology. 2015;5:1-5.
57. S Y, Reeve J. A Meta-analysis of the effectiveness of intervention programs designed to support autonomy. Educat Psychol Review. 2011;23(1):159-188.
58. Imai K, Keele L, Tingley D. A general approach to causal mediation analysis. Psychol Methods. 2010; 15:309-34.
59. Hayes AF. Beyond Baron and Kenny: Statistical mediation analysis in the new millennium. Communication Monographs. 2009;76 (4):408–20.
60. MacKinnon DP, Luecken LJ. Statistical analysis for identifying mediating variables in public health dentistry interventions. J Public Health Dentistry. 2011;71:S37-S46.
61. Rucker DD, Preacher KJ, Tormala ZI, Petty RE. Mediation analysis in social psychology: Current practices and new recommendations. Social and Personality Psychology Compass. 2011;5/6:359–71.
62. Hayes AF. Introduction to mediation, moderation, and conditional process analysis: A regression-based approach, 2nd ed. New York: Guilford Press, 2017.
63. Little RJA, Rubin DB. Statistical analysis with missing data, 2nd ed. New York: Wiley, 2002.
64. Gansky SA, Neuhaus JM. Missing data and informative cluster sizes. In; Statistical and Methodological Aspects of Oral Health Research, E Lesaffre, J Feine, B Leroux, D Declerck, eds, Wiley, 2009, pp 241-257.
65. Plutzer K, Mejia GC, Spencer AJ, Keirse MJNC. Dealing with missing outcomes: Lessons from a randomized trial of a prenatal intervention to prevent early childhood caries. Open Dentistry Journal, 2010;4:55-60.
66. Rubin DB. Multiple imputation after 18+ years. J Amer Statist Assoc. 91:434:473-89.
67. Schafer JL. Multiple imputation: a primer. Stat Methods Med Res 1999;8:3-15.
68. Wagner Y, Greiner S, Heinrich-Weltzien R. Evaluation of an oral health promotion program at the time of birth on dental caries in 5-year-old children in Vorarlberg, Austria. Community Dent Oral Epidemiol. 2014;42;160–69.

69. Ghosheh J, Weber-Gasparoni K, Drake D, Warren J, Reeve, J, Xu J, Dawson D. Maternal behavioral changes in WIC toddlers facilitated by self-determination theory. 61st Annual session of the American Academy of Pediatric Dentistry, May 22-26, 2008.
70. Weinstein P, Harrison R, Benton T. Motivating parents to prevent caries in their young children: one-year findings. J Am Dent Assoc. 2004;135(6):731-8.
71. Ismail AI, Ondersma S, Jedele JM, Little RJ, Lepkowski JM. Evaluation of a brief tailored motivational intervention to prevent early childhood caries. Community Dent Oral Epidemiol. 2011;39(5):433-48.
72. Harrison R, Benton T, Everson-Stewart S, Weinstein P. Effect of motivational interviewing on rates of early childhood caries: a randomized trial. Pediatr Dent. 2007;29(1):16-22.
73. Harrison RL, Veronneau J, Leroux B. Effectiveness of maternal counseling in reducing caries in Cree children. J Dent Res. 2012;91(11):1032-07.
74. Baron, R.M., & Kenny, D.A. (1986). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. Journal of Personality and Social Psychology, 51(6), 1173-82.