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Caries Management By Risk Assessment in Children

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Caries Management by Risk Assessment in Children

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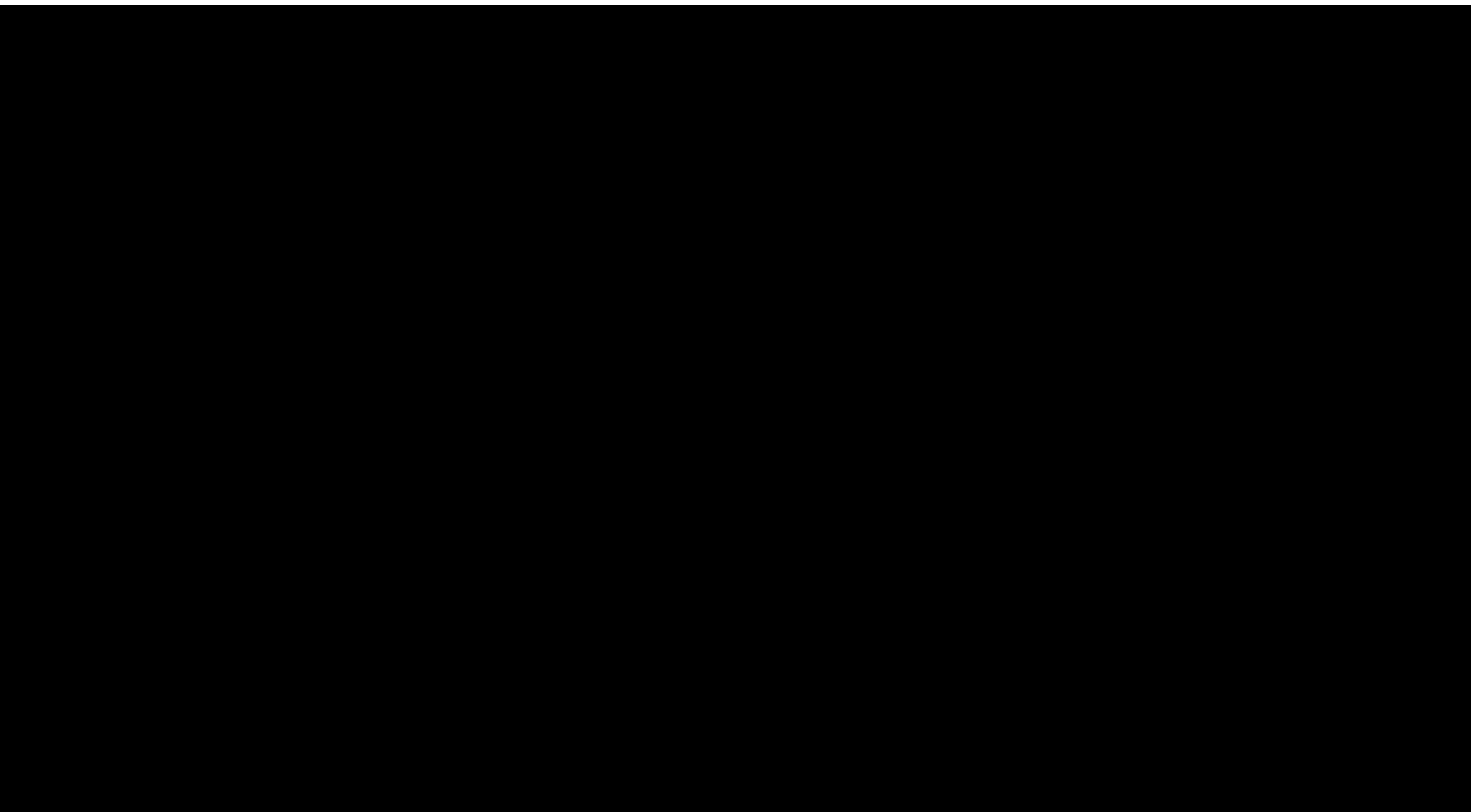

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Caries Management by Risk Assessment in Children

Niki Fallah

Abstract

Purpose: To evaluate the effectiveness of a modified Caries Management by Risk Assessment (CAMBRA) model in a clinical trial amongst children between the ages of 5-9 years old, treated in a school-based community pediatric dental clinic setting.

Methods: In a one-year, randomized clinical trial, 66 children between the ages of 5-9 years old were randomized into control or intervention groups. The control group received conventional treatment, including exam, prophy, caries risk assessment and fluoride varnish at baseline, 6 months, and one year follow up. The intervention group, in addition to receiving conventional treatment, also received CAMBRA, if considered high caries risk, which consisted of additional fluoride treatments at 3 and 9 months as well as daily xylitol mint consumption. Saliva samples for mutans streptococci (MS) and lactobacilli (LB) enumerations (CFU/ml) and dmfs/DMFS scores were collected from each subject at baseline and one year examinations.

Results: Of the 66 participants, 60 subjects completed the study. At baseline there was no statistical differences in subject demographics, MS and LB levels, along with DMFS/dmfs scores between the two groups. At six months and one year, there were no statistically significant differences in logMS and logLB levels between the two groups

(Student t- test p>0.05). Also, at one year, we did not find any significant difference in the change of decayed surfaces (DS/ds), smooth surface decay (SS-DS/ds) and overall decayed surfaces (DMFS/dmfs) between the intervention and the control groups (Student t-test, P>0.05). Although the difference is not statistically significant, the change of dental caries at one year in the intervention group displayed a consistent decrease in all scores compared to a consistent increase in the control group with a borderline statistically significant difference in SS-DS/ds (Student t- test, P=0.06). The caries risk assessment tools reviewed the oral habits of the children, such as oral hygiene and diet. An increase in tooth brushing frequency was reported from both control and intervention groups, with a decrease in snacking frequency per day. Although neither was statistically significant, it presents a positive trend towards a reduction of risk factors along with an increase in protective factors for both groups.

Conclusions: Although the modified CAMBRA intervention in children did not significantly reduce MS levels or change DMFS/dmfs scores, it did show positive trends towards reducing caries, especially on smooth surfaces. It has also shown decreased lactobacillus levels in children ages 5-9 years old. Due to limitations within the study, we were unable to recruit a sufficient number of subjects to meet the sample-size calculation. Future studies with sufficient number of subjects is needed to validate the success and positive benefits of the modified CAMBRA protocol in young children.

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1. Introduction:

As the most chronic disease affecting childhood, dental caries has preceded over other common pediatric conditions such as asthma and hay fever, occurring nearly five and seven more times respectively.[1] Dental caries affect not only a child's oral and dental development, but also has negative impacts on their social, emotional, and educational growth. Although a reduction of caries has been seen in recent years, more than half of all children in the US develop caries by the time they are in second grade and 80% by the time they finish high school.[2]

The third National and Health Nutritional Examination, or NHANES III, established a correlation between dental disease and particular racial and ethnic groups, with a strong prevalence amongst low-income communities.[3] Poor children suffer twice as many dental caries as their more affluent peers, and their disease is more likely to be untreated.[3] More than 36.8% of low-income children, aged 2-9 years, have one or more untreated dental decay in the primary dentition, compared to 17.3% of non low-income children.[3]

Many consequences can arise from neglected dental disease, such as intense pain and stress which leads to difficulties in eating, speaking, and missed days of school- amounting to more than 51 million school hours lost each year.[3] Pediatric oral disease has had a significant impact within society and the nation as a whole. In the U.S., the annual federal cost of treatment for pediatric dental caries is at least $4.5 billion.[1]

Recent data has shown that the presence of caries has significant ramifications on children and adolescents living in the US, impacting multiple facets of their life, and ultimately affecting their overall development into adulthood. With the progression of caries from the primary dentition into the permanent dentition, it has been suggested that 6-9 year-old children are at greatest risk for dental caries in mixed dentition, leading to caries well into adolescents and even adulthood.

A successful regimen that will break the cycle of this multifactorial infectious disease for high-risk children, will contribute greatly to provide good oral health not only for them now but also later in life.

2. Background and Significance:

Dental Caries and the risk from primary to permanent dentition

As an infectious disease, dental caries is considered pathologic and thought to be a multi-factorial process, which involves the dynamic integration of oral bacteria, saliva, enamel, dietary substrates, and many other factors.[4] The carious process has been thoroughly researched and is widely accepted. The main bacteria causing both enamel demineralization and lesion progression are Mutans streptococci (MS) and Lactobacilli (LB).[5]

Research has shown that MS are readily transmissible from one individual to the other, especially between caregivers and their children.[6] These bacteria are acidogenic, acidoduric and produce organic acids in the presence of fermenTable carbohydrates.[5] Producing glycoamino-glucans, which allows them to attach securely to the tooth's surface, these bacteria will colonize on enamel, causing a drop in pH when fermenTable carbohydrates are consumed. Consequently, as more acid is produced, breakdown of the enamel carbonated hydroxyapatite structure will occur and eventually lead to significant demineralization of the tooth's enamel structure. This process has left the enamel structure vulnerable to future acid attacks, eventually causing irreversible cavitation to the tooth's structure. [4,5]

Furthermore, the NHANES III study 1999-2002 demonstrated caries risk being carried over from primary/mixed dentition to the permanent dentition. The data showed the prevalence of dental caries was 49.0% and 20.1% in deciduous and permanent teeth respectively among 6-11 year-old children, while 12-15 year-old adolescents showed 49.6% of caries prevalence in permanent teeth.[7] These results highlight the severity and direct correlation of how caries present in the primary dentition has a strong association to caries in the permanent dentition.

Caries Prevention

Diet

A child's diet plays a crucial role in the development of caries and is thought of as one of the main risk factors, especially sugar and fermenTable carbohydrate intake.[8] Common food items found in the diet of U.S. children contain high levels of both sugar and other fermenTable carbohydrates. These include but are not limited to: juice, soda, chips, crackers, cookies and fast food items.[9] Upon eating and drinking, as well as afterwards, the plaque on the teeth drops in pH due to the production of lactic acid, acetic acid and other acids, which results from MS and LB metabolizing the residual food particles left in the mouth.[10] A published review in 2003 concluded that the drop in pH occurs quickly post sucrose consumption, with the strongest acidic environment evident within minutes of sucrose ingestion.[11] It was also determined that pH recovery did not occur as quickly, taking between fifteen to forty minutes- depending to a large extent on the acid buffering and clearance properties of the individual's saliva.[11] Caries causing bacteria can metabolize sucrose with greater ease and efficiency, resulting in a rapid drop in pH. Other fermenTable carbohydrates on the other hand take more time integrating into plaque and require additional steps of being broken down prior to bacterial metabolism. This process creates a stagnant and lingering acidic environment for the bacteria after ingestion.[11]

A plaque pH of 5-6 initiates the breakdown of enamel and consequently the caries process. The frequency and type of cariogenic foods ingested are the primary factors in establishing and maintaining the optimal setting for MS and LB. The microbial composition of the tooth biofilm and saliva factors plays a crucial role as well. Repeated and continued exposures to cariogenic foods keeps the pH at acidic levels, resulting in weakened and broken down enamel, ultimately leading to caries formation, cavitation and irreversible tooth structure damage.[4]

The consumption of excess carbohydrates and fats not only serve as high risk factors in the caries process, but are also a major contributor to poor systemic health, including malnutrition and obesity.[11] The US Department of Agriculture and the Department of Health and Human Services have raised awareness towards the overall health decline and obesity epidemic in the US by establishing clear dietary guidelines.[12] Oral and health care professionals have long supported these recommendations, educating patients on healthy habits and food choices. These suggestions are not only efforts towards improving overall health, but also a method of caries prevention. Even though health care providers have a professional responsibility in educating their patients along with discussing possible risks and outcomes, patient compliance is not always practiced in maintaining an overall healthy life and diet, especially in children.[13]

This has become most evident within the past few decades, as childhood obesity has more than tripled in the United States. The outbreak of overweight children and youth is now considered a critical national health threat.[14]

With dental caries being considered one of the most dominant chronic diseases in children and obesity rates climbing at staggering rates close behind it, many pediatric dentists now calculate BMI scores and record it as part of the child's dental record.[15] Although there have been no published studies in the US identifying the two as having a direct cause and effect relationship, it has been suggested that it may contribute towards one another.[15] Some studies have suggested that they may simply coexist due to their etiological factors of diet and socioeconomic status. In addition, one can hypothesize that due to a cariogenic diet, containing high sugar and carbohydrate content, obese children are more likely to have an increase of caries incidence versus children who are in the normal or lower weight categories.[14]

Willerhausen et al (2004) found a distinct correlation between high levels of caries amongst overweight and obese German children.[16] As well as Alm et al (2008) who studied over 400 Swedish children and argued that overweight and obese adolescents had more proximal caries.[16] At present time, more literature has revealed varied associations between childhood overweight/ obesity and caries, leaving one to assume that the relationship between weight and caries is multi-factorial and complex.[17] For oral health care providers, this becomes a significant problem as a child's obesity status plays a key factor in determining safe treatment options when treating caries.

Presently, the American Dental Association as well as the American Academy of Pediatric Dentistry has established guidelines for children of all ages and weight.[18] These suggestions are backed by studies, which clearly show that proper and

reasonable dietary modifications, including healthy foods and a reduction of the frequency and duration of high sugar or carbohydrate diets, can decrease the incidence of caries.[19]

The recommendations suggest eating a balanced diet rich in whole grains, fruit and vegeTables, along with good and consistent oral hygiene. It also states eating certain foods together, rather than individual snacks, such as combining dairy products and fermenTable carbohydrates and other sugars, which can reduce the risk of caries and erosion. Furthermore, adding raw fruit or vegeTables to meals increases salivary flow, as well as choosing water over acidic or sugary soda's and beverages.[20]

Educating the child and parent on proper diet and oral hygiene practices with the hope such information will positively influence future behavior, not just for oral health but for overall systemic benefits, is a primary goal of any preventative regimen. As we know, a combination of aggressive preventative regimens including antimicrobial therapy, fluoride therapy, oral hygiene and diet counseling can significantly reduce the new caries incidence in a high risk adult population; greater efforts should be made in establishing preventative regimens and healthier diet habits for the pediatric patient, as a measure to prevent future oral and systemic disease.[21]

Sealants

Resin based dental sealants on pits and fissured surfaces have shown a significant reduction of caries on permanent molars.[22] Children and adolescence have shown positive results in caries reduction, with 86 percent after one year and 65 percent after nine years of sealant placement.[23] As a cost effective and minimally invasive preventative measure, dental sealants have shown to have good longevity and success with proper maintenance and monitoring.

Dental sealants have been increasingly utilized in children with permanent molars since it first became available in the 1970's. According to NHANES however, significant disparities remain in some populations, despite the improvement. Only 30% of children 6-11 and 38% of adolescents 12-19 have dental sealants- with younger children, Black and Hispanic children, and those living in families with lower incomes being least likely to having them.[24]

Fluoride

Fluoride has been used in the United States as an anti-caries prevention method for over forty years. Many different forms of fluoride delivery are available, including dentifrices, rinses, gels, public water supply, and most recently as a varnish. Although it

has previously been used as a desensitizer for many years, it has only up until recently been used as a topical medicament for caries prevention.[25]

Despite much of the research supporting fluoride varnish as an effective topical anti-caries treatment; it is currently not approved by the FDA as any other agent other than a Class II Medical Device for use as a cavity liner and/or tooth desensitizer and considered "off label" for caries prevention.[26,27]

Fluoride varnishes comes in 1%-5% Sodium Fluoride and Difluorsilane concentrations in a resin or polyurethane base. Once placed on the tooth's surface, the varnish hardens upon coming into contact with saliva, releasing fluoride ions.[28] The process of remineralization is then initiated, where the adhered fluoride releases over a period of time (1-7 days). One of the benefits of fluoride varnish is the ease of application along with prolonged benefits with minimal systemic ingestion and adverse effects.[26]

The American Dental Association along with the American Academy of Pediatric Dentistry have recognized fluoride varnish as an effective method of caries reduction and include it in there guidelines for periodic exams. Studies have shown that children receiving professional fluoride treatments every six months can reduce DMFS scores by 18.3%.[29]

Fluoride varnish holds many benefits over other forms of topical applications. It provides a fast and simple delivery method, with minimal risks for systemic ingestion while

maintaining prolonged fluoride release. High-risk populations, especially those from low-income families, can greatly benefit from this cost effective preventative measure in maintaining oral health and minimizing the occurrence of caries, particularly in the primary dentition.[30,31]

Chlorhexidine

Chlorhexidine gluconate mouth rinse is a chemical antiseptic with bactericidal and bacteriostatic actions on both gram-positive and negative bacterial species. It significantly reduce levels of MS, (LB to a lesser degree), as well as overall plaque levels with long term use. The mechanism of action has been shown to be a disruption of the bacterial membrane.[32] Chlorhexidine has both immediate and prolonged effects on these oral bacterial species by binding and absorbing into the tooth pellicle.[33] Both invitro and in vivo studies have shown chlorhexidine's ability to disrupt plaque formation and alter concentrations of MS. It's particularly effective when combined with fluoride therapy.[34]

Chlorhexidine has been approved by the FDA for nearly thirty years, and has been shown to be safe with no serious negative side effects. However, prolonged use has been reported to cause extrinsic tooth staining- along with the unpleasant taste reported by its users. Although its effects against caries causing bacteria has a strong correlation, its influence on the actual reduction of caries as well as lowering one's risk

for future dental decay, has limited scientific support and needs further investigation to establish a direct relationship.[34,35] One recently published study in high caries risk adults by Featherstone et al., showed marked reductions in MS and a 24% reduction in new DMFS over a 2 year period when chlorhexidine was used in conjunction with fluoride toothpaste and fluoride mouthrinse.[34]

As previously mentioned, chlorhexidine has a bitter and intense flavor, making it unpleasant for children and consequently making compliance for consistent use difficult. Also, one must supervise children while using this mouth rinse to minimize the risk of swallowing. Due to these concerns, it is not routinely utilized in this population as part of a long term, daily at home antimicrobial regimen for pediatric patients.

Xylitol

A key feature in sugar alcohols is their noncariogenic quality- where its consumption does not promote tooth decay.[36] Chemically, xylitol is a five carbon sugar alcohol, unlike its other polyol counterparts, sorbitol and mannitol, which contain a six carbon chain. A key feature of xylitol is the protective effects and its ability to reduce tooth decay by lowering levels of MS in plaque and saliva and reducing the level of lactic acid produced by them.[36] Specifically, it is “absorbed and accumulated intracellulary in S mutans. Xylitol competes with sucrose for its cell-wall transporter and its intracellular metabolic processes. Unlike the metabolism of sucrose, which produces energy and promotes

bacterial growth, S mutans expends energy to break down the accumulated xylitol without yielding energy in return. Furthermore, the energy-producing intermediates are consumed and not reproduced by xylitol metabolism." [37]

Additionally, xylitol has a number of other effects on S mutans that contribute towards caries reduction. Short-term consumption of xylitol is associated with decreased S mutans levels in both saliva and plaque. Long-term habitual consumption of xylitol appears to have selective effects on S mutans strains.[37] This results in selection for populations that are less virulent and less capable of adhering to tooth surfaces and, thus, are shed more easily from plaque into saliva. This is not only important for the individuals decay experience but also influences the transmission of S. mutans from mother to child.[36]

Xylitol is well tolerated by adults and children with minimal side effects, primarily causing intestinal discomfort and osmotic diarrhea if eaten in large quantities. Discomfort following the ingestion of xylitol has been reported in patients who have consumed 3-40 grams per day.[38,39]

Much of literature states that 5 to 6 grams at 3 exposures daily from either chewing gums or candies is needed for adequate S. mutans reduction where clinical effects can be achieved.[40] Increased levels of intake do not result in greater reduction in incidence of caries and may lead to diminishing anticariogenic results.[41] In 2006, Milgrom showed in a randomized controlled trial the does response of S. mutans in plaque and

unstimulated saliva to xylitol gum. His results revealed that the dosage of xylitol, in fact, had a ceiling effect in reducing S. mutans level, making higher (10.32g xylitol/day) and lower (3.44g xylitol/day) dosages less effective compared to moderate dosages (6.88g xylitol/day).[42]

Currently, xylitol can be found in many forms including foods, candy, gum, lozenges, Tablets, syrups, and even towelettes for infants.[43] Xylitol has become widely available with the potential of becoming accessible to consumers to enhance oral health. Determining if products contain adequate amounts of xylitol surrounds much controversy, as xylitol content is usually not clearly labeled and usually does not contain the required amount for proper caries prevention and S. mutans reduction.[36] Also, creating xylitol products that consumers are likely to purchase and ingest raises some challenges, especially amongst young children. According to current data, there are no safe xylitol products commercially available in the U.S. for infants and toddlers who are too young to chew gum.[36]

At the University of Washington, researchers have tested new xylitol-containing items that children are most likely to consume, such as popsicles, gummy bears, puddings, macaroons, and sorbet. [43] Children appear to accept such foods when given as a part of their daily diet. Future studies require the testing of snack foods on children to establish their effectiveness in preventing decay, as some foods are better at delivering and releasing xylitol than others.[43]

One of the greatest milestones in the research of xylitol and dental caries included the Turku Sugar Studies, which took place in the early 1970's.[44] Adult subjects had total substitution of almost all dietary sugars with xylitol for two years and were examined for any developments of dental caries. The daily consumption of xylitol was approximately 50g/daily, with results showing minimal caries development, compared to other groups taking fructose and sucrose.[45]

The major side effects described in this study were softening of stool and/or osmotic diarrhea in certain individuals whose intake was over 45g daily. For these side effects to occur, about four to five times the amount needed for the prevention of dental caries must be consumed.[46]

Since then, xylitol studies have been partial substitution or chewing gum supplementation studies, and have heavily focused on transmission levels from mother to child and caries prevention in the primary dentition.

In 2001, Soldering showed that habitual xylitol consumption by mothers had a strong correlation with a statistically significant reduction in the probability of mother–child transmission of S. mutans. Results were re-evaluated four years after the maternal xylitol consumption had been discontinued; and still displayed low levels of mutans streptococci in the children's' oral flora.[47]

Additionally, a study conducted in the Marshall Islands measured the efficacy of xylitol syrup on toddlers and infants. Children were placed in one of two treatment groups, xylitol syrup taken either 2x or 3x daily, or a control group receiving a very low dosage of xylitol 1x/daily. Both treatment groups received a total of 8g of xylitol/daily. The results of this study showed that xylitol had an effect during primary tooth eruption and could prevent up to 70% of caries when exposed to 8g of xylitol in twice-daily topical oral syrup. Dividing the 8g into three doses did not increase the effectiveness of the treatment. The study holds a great deal of significance as it provides evidence for the first time that xylitol is effective in the prevention of decay of the primary dentition in the teeth of infants and toddlers.[37]

Lastly, the most modern form of xylitol was recently studied in 2009. Using 44 mother-infant pairs in a double-blinded randomized controlled clinical trial, researchers assessed the efficacy of three times daily use of xylitol wipes in 6-35 month-old children with high caries risk. Mothers were instructed to use 2 wipes 3 times daily to swab their infants' teeth and gums. The result showed a significant reduction in new decayed surfaces in children after 1-year use of xylitol wipes compared to the placebo group. The data also indicated that MS genotypes were less likely to be retained in the xylitol group, suggesting that xylitol modifies MS colonization.[48]

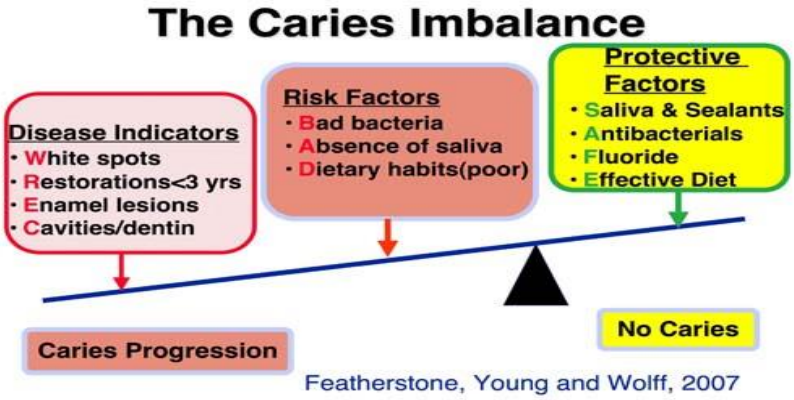
The unique characteristics and effects of xylitol make it a key component in the line of prevention of dental caries and maintenance of oral health. Unfortunately, most likely due to expense, the small quantity of xylitol in these items have little clinical benefit.

With continued research and the development of more products containing xylitol, one can assume that the demands of customers will be met and greater access to xylitol will be available. With clinically beneficial amounts of xylitol in every day products, the oral health of children and their parents can vastly improve, placing greater efforts towards caries prevention and aiming at lowering one's overall risk for future caries.

Caries Management By Risk Assessment

It is well accepted that the process of initiation, progression, and reversal of caries is a balance between several factors. This includes generated acid from caries causing bacteria due to metabolism of carbohydrate substrates from diet, a combination of demineralization inhibition, remineralization by protective factors (such as saliva, calcium, phosphate and fluoride), and antimicrobial treatment.[4, 10] (Figure 1).

Figure 1: Caries Balance Model



In order to reverse or break the caries cycle, protective factors must counterbalance risk factors, which lead towards caries progression. There have been four primary protective factors that have been recognized to successfully tip the balance towards a reduction of, or no, caries. These include: decreasing cariogenic bacteria by antibacterial treatment, enhancing remineralization with fluoride, and increasing salivary function. Identification of risk factors that imbalance the caries equilibrium and protective factors that restore the caries balance is the key for caries prevention.[4, 10,49]

In a 3-year randomized, controlled clinical trial in adults (aged 18-65 years), conducted at the University of California, San Francisco Dental School, provided clinical evidence that the use of a novel, scientifically based caries risk assessment tool in conjunction with aggressive preventive and therapeutic measures will restore the balance between pathological and protective factors in adults (Caries Management by Risk Assessment-CAMBRA).[34,50]

At each exam appointment, critical clinical and bacterial evaluation of “disease indicators” in conjunction with “risk factors” and “protective factors” are documented and then used to develop a caries risk level for each patient (Appendix 1). The assigned level of risk will determine which CAMBRA Clinical Guidelines the practitioner will recommend in order to determine the best regimen for caries reduction and/or prevention.

The results of this study revealed that an intervention with chlorhexidine gluconate (0.12%) and fluoride rinses (0.05% NaF) effectively reduced the cariogenic bacterial challenge, successfully reduced the caries risk status, and favorably altered the caries balance.[4, 10, 50] It also increased the percent of patients with few or no new caries.

The guidelines proposed by Caries management by risk assessment (CAMBRA) has shown to been successful in significantly reducing dental caries compared to conventional care in adult patients, 18 years and older.[50] In combination with therapeutic interventions, caries risk assessment has reduced the necessity for restorative treatment when compared to conventional adult treatment. The CAMBRA model has yet to prove the same results for pediatric patients.

Treatment Modalities in Children:

Preventative interventions are most critical during childhood years, primarily between the ages of 6-9, as it has been shown that caries in the primary dentition is a good predictor for caries in the permanent dentition.[51] During this time a child develops appropriate dietary and oral hygiene routines and can establish healthy habits that can be sustained later in life. Most importantly, therapeutic measures to prevent decay above and beyond the standard “brush and floss” recommendations are limited in this age group as compared to adults.

As stated earlier, CAMBRA guidelines for adults at high caries risk include the use of chlorhexidine and/or high concentration fluoride toothpaste (5,000 ppm F) home treatments. The use of chlorhexidine mouth rinses to control MS infections in children is not common due to the dissatisfaction with taste and causing a lack of compliance. Additionally, high concentration fluoride toothpaste poses a risk for fluorosis in the permanent dentition from over-ingestion.

If products such as xylitol, as antimicrobial treatments, are introduced and used by patients, the oral microbial composition can be modified- reducing cariogenic bacteria levels. This can rebalance the caries equilibrium and arrest the cycle of caries development in permanent dentition. A successful regimen that will break the chain of this multi-factorial infectious disease process, will contribute greatly to good oral health in children's immediate and later life.

CAMBRA guidelines for adults are currently recommended for children over 6 years old.[52,53] However, no study has been conducted to validate the efficacy of this regimen in children. Thus, studies are needed to evaluate this model of caries risk assessment and caries management methods in children between the ages of 6-9.

3. Aims, Significance, and Hypothesis:

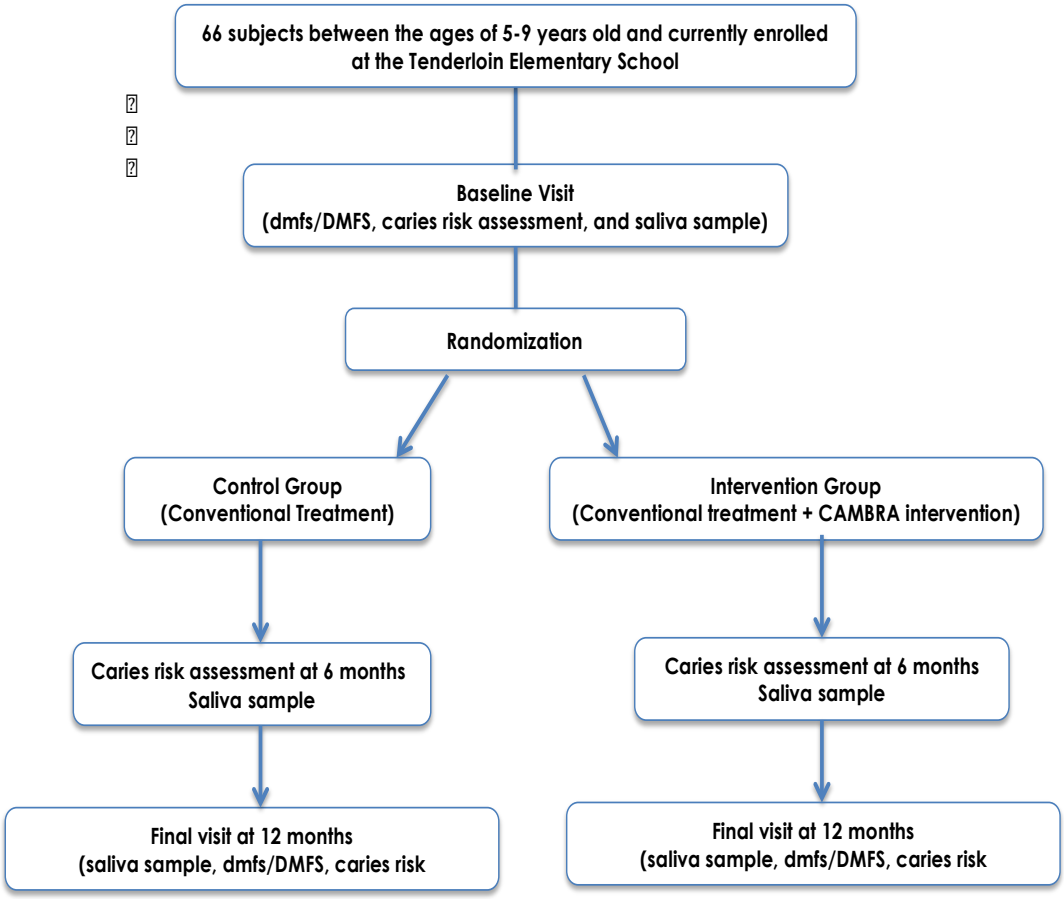
The aim of the study was to evaluate the efficacy of a modified Caries Management by Risk Assessment (CAMBRA) model in a clinical trial in children aged 6-9 years treated in a school-based community pediatric dental clinic setting. Specifically, we set out to reduce the bacterial load of MS and LB, along with improving the overall hygiene and dietary habits of subjects compared to control treatment, through restoring the balance between pathological and protective factors along with conservative restorations. We hypothesize that the CAMBRA protocol will significantly reduce the cariogenic bacterial load (MS & LB) in the intervention group as well as improve their oral hygiene care, and dietary habits as compared to the control group. Ultimately, it is hoped that utilization of a CRA tool and applied preventative regimen will lead in a reduction in bacterial load, improvement in dietary and oral hygiene habits with a concurrent short-term and long term decrease in future caries prevalence within this population.

4. Materials and Methods

1. Subjects and Study Design

The study was approved by the Committee on Human Research at University of California at San Francisco (CHR approval number 10-02176 March 16, 2010). The summary of study design is illustrated in Figure 2.

Figure 2: General Study Design



The sample size is based on the patient records from the UCSF Pediatric Dental Clinics during the past three years: 48% of patients needed at least one new restoration within one year after the completion of the initial treatment. We have chosen a more conservative figure of 40% for the control group. The previous xylitol wipe study had shown a 30% reduction in subjects with new caries in one year. With 59 patients in each group at final visit, we will have 80% power at 5% type 1 error for a two-sided test to detect the difference between a control caries proportion of 0.40 and a test caries

proportion of 0.10. With an estimated drop-out rate of 10% in the study, we will need to recruit 65 subjects per group (total subjects N=130). A total of 66 subjects ages 5 to 9 years old who attended the Tenderloin Community Elementary School and Dental Clinic between April 2010 to June 2012 were recruited into the study after meeting eligibility requirements.

Inclusion criteria required that subjects maintained being of record at the Tenderloin community or UCSF pediatric dental clinics throughout the duration of the study. They must be between the ages of 5-9 years old, able to give informed assent, consent and answer questionnaires in English, Spanish or Chinese by parents or guardian, and unlikely to move from the area during the study period. Lastly, they would need to be willing to participate regardless of group assignment and comply with all study procedures.

Exclusion Criteria were children who had prolonged antibiotic use in the past three months or dental needs outside of the community pediatric clinics, which would require treatment in specialty clinics.

Drs. Zhan, Johnson or Fallah explained the study, possible risks and benefits as well as answered questions to potential participants and their guardians in person or via telephone. Parents and guardians were also given detailed, written information packets which full outlined the study, which included study goals, participation responsibilities,

risks and benefits as part of the consent process. Written informed assent and consent (approved by the UCSF CHR) was obtained from the participants and their guardians.

Upon enrollment subjects were randomized into either the intervention or control group. If siblings were enrolled in the study, all later enrolled siblings were assigned to the sample group as the first enrolled sibling. Each subject, regardless of assignment, then had an initial examination performed, a DMFS/dmfs (permanent and deciduous teeth respectively) score recorded using NIDCR caries diagnostic criteria, saliva samples, and caries risk assessment recorded.

The control group received the current conventional preventative and restorative therapies as indicated by the UCSF Pediatric Dentistry Clinic and AAPD guidelines. All children received full mouth dental prophylaxis and fluoride varnish treatment every six months. General oral hygiene instructions i.e. observed (or completed by parent) twice daily tooth brushing with fluoridated tooth paste, flossing one time per day, healthy diet with limited in-between meal snacking were given to children and their parents. Sealants were placed on permanent molars, which have deep pits and fissures and restorative dental therapy as indicated due to dental caries.

The intervention group received conventional dental treatment (same as the control group) in conjunction with CAMBRA preventative therapies and recommendations based on the subject's caries risk status (Figure 3).

Caries risk status was determined by evaluation of four criteria: disease indicators, risk factors, protective factors and salivary MS and LB levels. Once caries risk criteria were determined, the subject was then classified as low, moderate, high, or extreme risk based on these results (Appendix 1).

Risk categories are based as follows: “High Caries Risk” refers to subjects with one or more of the disease indicator criteria: active caries lesion(s) to dentin, a proximal enamel lesions by radiograph, white spots on smooth surfaces or restorations in the last three years. “Low Caries Risk” included subjects with no disease factors and minimal risk factors that are well balanced with protective factors. “Moderate Caries risk” comprised of individuals without any of the disease indicators, but with predominance for risk factors in combination with minimal utilization of protective factors. Moderate risk is thus more arbitrary and limited to clinician subjective expertise.

Figure 3: CAMBRA Clinical Guidelines for Patients 6-9 years Old

Risk Level	Home fluoride use & professional fluoride visit	Xylitol and/or Baking Soda
Low Risk	Home use regular fluoride toothpaste 2x daily.	Not indicated
Moderate Risk	Home use regular fluoride toothpaste 2x daily. Fluoride varnish every 6 months.	Four xylitol mints 3-4 times daily.
High Risk	Home use regular fluoride toothpaste 2x daily. Fluoride varnish every 3 months.	Four xylitol mints 3-4 times daily.
Extreme Risk	Home use regular fluoride toothpaste 2x daily. Fluoride varnish every 3 months.	Baking Soda rinse 4-6 times daily. Two xylitol mints 3-4 times daily.

The caries examiner (LZ) was blinded to the caries risk status and the group assignment of the subjects. Caries risk status was not made known to the study participants, caries examiner or the dental care providers until the end of the study. The caries risk status was reported to the parents or guardian of the patient along with the home care instructions for both groups. Preventive regimens in addition to the standard dental care protocol were delivered to these subjects based on their caries risk status according the modified CAMBRA guidelines (Figure 3).

1. Low risk individuals received the usual standard dental care provided at the clinics, including general oral hygiene instruction, cleanings and restorative work with recommendation to floss once per day, brush two times daily with over the counter fluoride toothpaste, and diet consultation.
2. Moderate risk individuals received the same education and treatment as low risk individuals with the addition of professional fluoride varnish application every six months and xylitol mints for home use (4 mints 3-4 times per day with a maximum dosage of 6-8g per day).
3. High risk individuals were treated equally to moderate risk individuals except with the addition of increased professional fluoride varnish application every three months.
4. Extreme risk individuals were treated equally to high-risk individuals except with the addition of baking soda rinse 4-6 times daily.

All subjects received restorative dental treatment as necessary within the first six months of enrollment as well as six month caries risk assessments, exam, dental

cleaning, oral hygiene instruction, topical fluoride application and bacterial saliva samples.

Intervention group parental handouts (modified adult CAMBRA guidelines, see Appendix 3) which discusses the mechanisms of the carious infection and transmission process, as well as oral hygiene and diet recommendations in lay terminology were sent home with subject at the baseline exam. A quarterly parental questionnaire was sent home with each subject to ask questions regarding use of xylitol mints, noted side effects (see attached quarterly questionnaire appendix 3). If the questionnaire was not returned or the guardian has any questions regarding the study protocol or side effects, they were contacted by the study coordinator.

Saliva Collection

Two ml of paraffin-stimulated saliva was collected from each subject at the initial and six-month visit prior to any of the clinical procedure and at least one hour after eating and tooth brushing. Saliva samples were stored and transported to the lab facility on ice and analyzed within 24 hours of collection.

Microbiological Assays

Cariogenic bacterial levels including MS, LB, and total viable bacterial in saliva were measured by culture on mitis salivarius sucrose bacitricin agar, Rogosa tomato juice

agar, and sheep blood brain heart infusion agar respectively. All saliva samples from each appointment were handled in an identical fashion and processed within twenty-four hours of collection. The saliva samples were sonicated for 20 seconds prior to preparing a 10-fold serial dilution series (10-1 through 10-5) in phosphate buffered saline (PBS). One-tenth ml of each saliva sample dilution was plated on MSSB and on Rogosa Tomato Agar. The plates were incubated anaerobically (85% N2, 5% CO2,10% H2) at 37ºC for 72 hours for subsequent enumeration of MS, LB, and TVC colonies using a dissecting microscope. The bacteria levels were recorded as colony forming unit. Enumeration was blind to subject group assignment.

Data Analysis

All data was entered into a computerized database. Descriptive statistics (mean, median, standard error, interquartile range, minimum and maximum) of the responses tabulated for each group at each time point measured. Demographics, compliance, questionnaire items for the two treatment groups were compared using Fisher exact tests, chi-square tests, t-tests, and Wilcoxon rank sum tests, depending on the scale of the item. All statistical tests were conducted at 0.05 significance level. Salivary components (MS, LB) for the two groups were log transformed and compared between the modified CAMRA and regular treatment groups at six months with linear mixed effect model to account for the correlation between siblings within a family adjusting for baseline values.

Caries risk assessment variables at six months were compared between the modified CAMRA and regular treatment groups with generalized estimating equation models to account for the correlation between siblings within a family while adjusting for baseline values, where logit link was used for dichotomous risk categories and cumulative logit was used for ordinal risk categories.

5. Results

Baseline demographic, caries status and bacteria levels:

A total of 66 children between the ages of 5-9 years (mean age 6.8 +/-1.55 years) were recruited for the study with 31 males and 34 females; by the end of the study, six subjects had dropped out. The baseline demographics are displayed in Table 1 below. The majority of subjects were Hispanic (47%), followed by Asian (33%), Caucasian (5%), African American (5%), Pacific Islander (5%), other (5%), and Native American (2%). The study consisted of 9 sets of siblings, with one set of triplets. Siblings were purposely placed together in the same treatment group (intervention or control) and randomized accordingly as a single unit to limit complications or cross contamination within families with regards to xylitol therapy and oral hygiene/diet instructions. At baseline there were no significant differences amongst the control and intervention groups in regards to age, gender, bacterial level and other clinical variables (Table 1).

Table 1: Baseline Demographics

	Control n= 31	CAMBRA n= 35	Tests P values
Age (Mean ± SD)	7.0 ±1.5	6.8 ±1.5	Student t-test 0.70
Gender M/F	14/17	17/18	Chi-square 0.78
Ethnicity: AA/AS/C/H/PI/N/O*	1/13/0/12/1/1/3	2/9/3/19/2/0/0	Chi-square 0.14

*AA= African American; AS= Asian; C= Caucasian; H=Hispanic; PI= Pacific Islander; N= Native American

There were no statistically significant differences at baseline when comparing bacterial levels (log MS, log LB, and log TVC) as well as total tooth surface (tts), decayed surfaces (DS/ds), smooth surface decay (SS-DS/ds), or overall decayed, missing of filled surfaces (DMFS/dmfs) (P>0.05) between the two groups as presented in Table 2.

Table 2: Baseline bacterial levels and caries data

	Control n= 31 mean +/- SE	CAMBRA n= 35 mean +/- SE	P values Student t-test
Log MS	4.0 +/- 0.4	4.5 +/- 0.3	0.34
Log LB	1.8 +/- 0.4	1.9 +/- 0.4	0.87
Log TVS	8.5 +/- 0.1	8.4 +/- 0.1	0.86
DMFS/dmfs	15.0 +/- 2.5	15.1 +/- 2.3	0.99
tts	22.0 +/- 0.4	21.0 +/- 0.6	0.34
DS/ds	8.2 +/- 2.0	9.0 +/- 1.7	0.75
ss DS/ds	4.9 +/- 1.3	4.7 +/- 1.0	0.88

Microbiological Data at 6 months and 1 year:

There were no significant differences of bacterial levels (log MS, log LB, log TVC) at 6 months and 1 year, between the control and intervention group (P>0.5), as summarized in Tables 3 and 4. Within each of the groups, the bacteria levels also seemed to be sTable with very minimal changes (Table 3, 4).

Table 3: 6 month bacterial levels

	Control n= 28 mean +/- SE	CAMBRA n= 32 mean +/- SE	P values Student t-test
Log MS	4.40 +/- 0.30	4.20 +/- 0.36	0.69
Log LB	1.70 +/- 0.40	1.80 +/- 0.40	0.84
Log TVC	8.50 +/- 0.07	8.50 +/- 0.06	0.96
Delta Log MS from baseline to 6 months	0.40 +/- 0.44	-0.27 +/- 0.41	0.28
Delta Log LB from baseline to 6 months	-0.07 +/- 0.47	-0.07 +/- 0.39	0.99
Delta Log TVC from baseline to 6 months	0.08 +/- 0.08	0.06 +/- 0.07	0.82

Table 4: One-year bacterial levels

	Control n= 29 mean +/- SE	CAMBRA n= 31 mean +/- SE	P-values student t-test
Log MS	3.60 +/- 0.41	4.10 +/- 0.42	0.48
Log LB	1.40 +/- 0.31	8.50 +/- 0.40	0.27
Log TVC	8.50 +/- 0.09	8.50 +/- 0.06	0.39
Delta Log MS from baseline to 1 year	-0.39 +/- 0.38	-0.33 +/- 0.47	0.91
Delta Log LB from baseline to 1 year	-0.39 +/- 0.45	0.16 +/- 0.46	0.40
Delta Log TVC from baseline to 1 year	-0.01 +/- 0.11	0.09 +/- 0.08	0.50

Caries status and caries increment at 1 year:

At one year, the changes in caries status were analyzed between both groups. The data does not reveal any statistically significant differences between the groups when comparing total tooth surface (tts), decayed surfaces (DS/ds), smooth surface decay (SS-DS/ds), or overall decayed, missing of filled surfaces (DMFS/dmfs) (P>0.05). However, a borderline decreasing trend in caries level was seen in enamel buccal and lingual DS/ds in the intervention group compared to control group (Student t-test, P=0.06). Table 5 displays the one-year caries data.

Table 5: One-year caries data

	Control n= 29 mean +/- SE	CAMBRA n= 31 mean +/- SE	P values Student t-test
1 yr DMFS/dmfs	13.70 +/- 2.20	11.90 +/- 2.00	0.55
1 yr tts	22.20 +/- 0.74	23.10 +/- 0.28	0.30
1 yr DS/ds	3.79 +/- 0.77	3.10 +/- 0.58	0.45
1 yr ss-DS/ds	3.00 +/- 0.78	2.10 +/- 0.47	0.28
DFS/dfs change	1.10 +/- 0.77	-0.35 +/- 0.64	0.14
DS/ds change	0.79 +/- 0.75	-0.65 +/- 0.65	0.15
ss-DS/ds change	0.62 +/- 0.68	-0.48 +/- 0.47	0.18
enamel pits and fissures DS/ds change	0.14 +/- 0.27	-0.03 +/- 0.21	0.62
enamel buccal and lingual DS/ds change	0.38 +/- 0.54	-1.03 +/- 0.49	0.06
interproximal DS/ds change	0.14 +/- 0.29	0.32 +/- 0.36	0.70

Attrition, Compliance and Adverse events

Throughout the entire study, all subjects met the inclusion criteria and were concurrently enrolled in both the Tenderloin Community Elementary School and affiliated UCSF/BAWCC on-site Dental Clinic. Six subjects withdrew from the study due to relocation/school transfer, causing a 9.1% dropout rate.

Compliance of xylitol-mint use at home was measured by a take home questionnaire completed by the parents at three, six, nine, and 12 months. At the three-month evaluation, only 25% of parents reported they were able to give equal or greater than 12 mints per day to their child as prescribed. The most reported difficulty was in giving mints to the child more than two times per day, skipping the afternoon dosage the most. The remainder of these parents reported they were giving the child either less than two or between 2-9 mints per day- despite being contacted by the study supervisor and reminded of instructions regarding mint quantity and frequency. By six months the mint compliance rates dropped to 12% as presented in Table 6. There were no aversive events reported associated with either fluoride or xylitol therapy aside from one subject who reported they didn't like the taste of the mints. At nine months, the compliance remained at 12%, while 70% received somewhere between 2-9 mints per day and 18.5% received less than 2 mints/day. At twelve months the compliance rate dropped even further to 6%, with 88% of subjects receiving 2-9 mints/day and 6% less than two mints/day.

Table 6. Xylitol Mint Compliance

	Questionnaires Reviewed	% Children that took 0-2 mints/day (under therapeutic dosage)	% Children that took 2- 9 mints/day (under therapeutic dosage)	% Children that took >/= 12 mints/day (therapeutic dosage)
3 months n= 24	24	25	50	25
6 months n= 25	25	28	60	12
9 months n= 27	27	8.5	70	12
12 months n= 15	15	6	88	6

Caries Risk Assessment Results:

Caries risk assessment was performed for each subject at baseline, 6 month, and one year visits. Key caries risk assessment at each appointment includes three areas of focus: Disease indicators, Risk factors and Protective factors. Disease indicators used in this evaluation included the placement of restorations less than three years. Risk factors include visualization of plaque, deep pits and fissures, inadequate saliva flow, saliva reducing factors (systemic or medications), and frequent snacking greater than three times per day (especially of fermenTable carbohydrates, sticky or high fructose laden items). Protective factors evaluated include frequency of tooth brushing, at home and professional fluoride, as well as unstimulated, adequate saliva flow (greater than one milliliter per minute). As shown in Table 7, there were no significant differences between groups at baseline for all risk assessment categories.

Overall, the caries risk factors show a decreasing trend in both the control and intervention groups when analyzing data collected at baseline, 6 months, and 1 year. At baseline 55% of subjects in the control group had restorations within the past three years, compared to 48% of the intervention group. At 6 months an increase in restorations was seen in both control and intervention groups, 79% and 75% respectively. By one year, both groups had all current cavitated lesions restored. The control group remained at 79%, while the intervention group increased to 87%.

When comparing risk factors such as the presence of heavy plaque, the control group showed an overall increase with baseline 45%, 6 months 46%, and 1 year 64%. The treatment group however showed an inconsistent trend in heavy plaque with baseline 60%, 6 month 44%, and one year 53%.

Snacking frequency declined in the control group from baseline to six months 41%-32%, but rose again at one year to 39%. The intervention group showed an overall decline from 52% to 49%, to 37% at baseline, six months, and one year. When analyzing deep pits and fissure caries the control group had an overall increase from 48% to 61% to 68% from baseline, six months, to one year. The intervention group showed a drop from baseline to six months, 58% to 53%, but went back up at the one year interval with 59%. Unstimulated saliva flow was adequate in all subjects except for two in the intervention group at the one-year mark. In addition, two subjects in the same group were on saliva decreasing medications at the beginning of the study, both of which discontinued the medications by the six-month interval.

Within the categories of prevention, including tooth-brushing frequency, a positive change was observed in both the control and intervention groups. Between baseline and one-year data results, reported brushing 1x per day decreased from 34% to 18% and 27% to 22% for both control and intervention groups respectively. As expected, the brushing 2x per day increased in the control group from 55% to 79%, and 58% to 78% in the intervention group. In both groups, professional fluoride application rates within one year increased substantially: controls went from 41% to 100% and the intervention group from 42% to 100% due to recall compliance. In addition, fluoride application was given in three-month intervals for high-risk caries patients in the intervention group. After being enrolled in the study, medium to high-risk patients in both the control and intervention groups had a rate of 100% fluoride varnish application. Overall caries risk categories stayed unchanged, as the majority of subjects were high caries risk at baseline with most having active caries lesions and requiring dental restorative care. See Table 7.

Table 7: Caries Risk Assessment Results

	CONTROL			INTERVENTION		
	Baseline #subjects (%) n=29	6 months #subjects (%) n=28	1 year #subjects (%) n=29	Baseline #subjects (%) n=33	6 months #subjects (%) n=32	1 year #subjects (%) n=31
Restorations <3yrs	16(55%)	22(79%)	22(79%)	16(48%)	24(75%)	28(87%)
Heavy plaque	13(45%)	13(46%)	18(64%)	20(60%)	14(44%)	17(53%)
Snacking freq >3x daily	12(41%)	9(32%)	11(39%)	17(52%)	15(47%)	13(39%)
Deep pits/fissures	13(45%)	17(61%)	19(68%)	19(58%)	17(53%)	19(59%)
Adequate unstimulated saliva	29(100%)	28(100)	28(100%)	33(100%)	32(100%)	31(97%)
Saliva decreasing medications	0(0%)	0(0%)	0(0%)	3(9%)	0(0%)	0(%)
TB Freq (%) 1xd 2xd	 10(34%) 16(55%)	 0(0%) 28(100%)	 5(18%) 22(79%)	 9(27%) 19(58%)	 7(22%) 26(81%)	 7(22%) 25(78%)
Pro Fl/Varnish(%) 0 1	 16(55%) 12(41%)	 0(0%) 28(100%)	 0(0%) 28(100%)	 19(58%) 14(42%)	 0(0%) 32(100%)	 0(0%) 32(100%)
Pro Fl/Varnish <6 months	12(41%)	25(89%)	25(89%)	14(42%)	30(93%)	30(93%)
Took xylitol mints	0(0%)	0(%)	0(%)	33(100%)	32(100%)	32(100%)
Overall CRA risk category High Medium Low	 26(90%) 2(7%) 1(3%)	 25(89%) 1(4%) 2(7%)	 25(90%) 3(11%) 0(0%)	 30(90%) 1(3%) 2(6%)	 29(90%) 2(6%) 1(3%)	 29(90%) 1(3%) 2(6%)

In order to accurately evaluate past, present and future caries susceptibility using the CAMBRA model, specific caries risk questions must be analyzed and measured. As stated previously, the focus was placed on specific subjective and objective criteria. The following categories were included in the overall evaluation of caries risk: placement of previous restorations within the past three years, visual presence of plaque during dental examination (either “yes” or “no”), subjective self-report on snacking frequency of > 3x/day to determine if subject engaged in pathologic snacking behavior, along with evaluation of pits and fissures with unstimulated saliva flow. The presence of these anatomical/physiologic markers can substantially increase caries risk status if the pits and fissures are deep (thus un-cleansable), and if observed, unstimulated saliva flow appears to be insufficient. Saliva decreasing medications include a multitude of prescription medications. The most commonly encountered in children are anti-psychotics, anti-depressants and stimulant based treatments for ADD and ADHD.

Additionally, tooth-brushing frequency was measured by self-report of child and was quantified into either no brushing, one time a day, and two times a day. Professional fluoride application was evaluated by the subjects recall frequency and based on overall CRA i.e. need for fluoride therapy. Adequate stimulated saliva flow was evaluated when taking saliva samples, and greater than one milliliter per minute is considered normal and not at increased caries risk. Lastly, overall caries risk status was evaluated for each subject at baseline, six months, and one year by rating all risk factors (disease indicators, risk verses protective factors).

6. Discussion

As an infectious disease, the cause of dental caries is multifactorial. Previous studies have shown the removal of caries and placement of restorations doesn't simply change caries risk[10]. Rather, the balance between a person's exposure to caries risk factors and preventive factors has the greatest influence on the presence of caries and caries risk. The paradigm of caries prevention must focus on management of caries risk factors, and subsequently reducing these factors and shifting the balance to preventive factors.[10] The aim of this current study was to investigate the practicality and efficacy of a modified CAMBRA protocol on cariogenic bacteria loading and modification on caries risk and prevention factors in 5-9 years old children in a community pediatric dental clinic.

The daily home consumption of xylitol mints was the main additional preventative measure in the intervention group regimen, to reduce or modify cariogenic bacteria in high-risk children. The instructed dosage of daily xylitol for each subject in the intervention group was 6-8g/day, which is considered a therapeutic dosage according to previous studies.[42] Our study revealed only a slight reduction of logMS and logLB in the intervention group with no significant differences to baseline or control group. Previous studies have consistently shown that short-term xylitol consumption decreases MS levels in both stimulated saliva and plaque while long-term xylitol consumption is thought to select out MS strains that are more easily shed from plaque into saliva.[55,56] The changes in bacterial levels of MS and LB after xylitol therapy have traditionally

been of short duration, anywhere between 4 weeks to six months. These studies clearly show a pattern of initial decrease in bacterial levels followed by a gradual return to baseline levels, plateauing around nine months.[54,57,58] It is thought the initial decrease followed by a return to baseline is due to selective Xylitol resistant strains of MS.[48,54,60]

In addition, for xylitol therapy to be effective in reducing MS and caries, subjects must take between 6-8 grams of Xylitol per day. A dependent relationship between the dosage/frequency of xylitol in controlling MS levels has been established. Milgrom et. al revealed there was a linear reduction in mutans streptococci levels in plaque and saliva with increasing frequency of xylitol gum use at a constant daily dose at intervals greater than two times per day.[48] We proposed in our study that the dosage and frequency of xylitol should be kept at 8 grams per day, divided into 3-4 intervals, morning, afternoon and evening, in order to reach a peak of effectiveness. Such medication compliance is thought to be reasonable and attainable for both short and long term therapy. However, the compliance of xylitol consumption in our study was low. The decreased daily intake amount and/or the frequency of xylitol mints could have compromised the caries inhibitory properties of xylitol therapy in our study.

The role of fluoride in caries prevention holds a great deal of significance, mainly by enhancing remineralization and inhibiting demineralization. The risk of fluorosis in 5-9 year old children is still present and can affect the developing posterior permanent teeth. The modified CAMBRA protocol for children however alters the adult regimen, by eliminating daily home high fluoride products and introducing more frequent in office

professional fluoride applications. This decreases the risk of fluorosis by keeping high fluoride products in a controlled environment where the systemic ingestion is kept to a minimum. In addition, given the specific setting of the dental facility in the school, professional application of fluoride had a better control of compliance than home use. The patient compliance would be assured which would be otherwise difficult if high fluoride products were consumed at home. The compliance of the fluoride varnish application schedule was ideal for both of the groups in the current study.

Recall and retention rates for test subjects within low income, inner city, non-English language speaking populations has been typically a huge challenge for public health researchers.[31] Not to mention, the no-show rates at community dental clinics are often as near 20-40% for scheduled dental appointments.[59] Thus, selecting a built in clinic/research site within an elementary school seems like an ideal and practical solution to maximize study recall rates as well as controlling dental therapy, while minimizing common limitations and challenges found within this demographic subject pool.

Overall, recall and follow up exam compliance were tightly controlled due to the clinic being on-site with simple and reliable access to test subjects. Subjects were easily retrieved from their class for dental exams, caries risk assessment, education, questionnaire and fluoride application. Our study showed that the in-office fluoride application rate increased dramatically from 42% to 100% in the intervention group and

41% to 100% in the control group.

Having a dental clinic on school premises within this population allows for significant advantages over standard community clinics delivery system. The first being in-school clinics can provide direct access to those children who are of biggest need of dental care without depending on parental compliance. Secondly, children miss much less classroom education time due to not having to leave the campus. Thirdly, parents do not experience any financial loss from missing hours from work or having to pay any travel expenses. Lastly, the dental team has much tighter control over recall and treatment because they are not relying on parental compliance. Thus, no-show or missed appointments were almost non-existent and treatment can be rendered nearly ideally, on schedule and in a timely manner.

Further analysis is needed to fully evaluate whether this type of in-house pediatric dentistry delivery system maximizes productivity, efficiency and effectiveness with regards to overall access and children's dental health within this population. It appears that such a model could be one of the most effective methods in addressing dental treatment disparities within this demographic, as dental providers have direct and reliable access to the children allowing them to manage their oral hygiene and treatment needs. This study clearly represents that, as our result shows that 100% of high-risk subjects received fluoride varnish per protocol at baseline, 6 months, and one year.

Oral hygiene and diet habits are critical factors in the caries balance model. In the current study, we included itemized handout to parents along with counseling to the children every three months, as a way to study whether this could be an effective method in the management of risk factors while promoting preventive behavior in high risk children. Although not statistically significant, the study did show a positive trend towards reduction of risk factors along with an increase in protective factors in both the control and intervention groups. Having restorations within the last three years is considered a significant disease indicator, and is a prime predictor for future decay. Our study revealed that within this population there is a high prevalence of unfilled caries and existing or previous restorations. This indicates that this population has a high incidence of caries, as seen from the initially high, and then dramatic increase in baseline previous restorations to one year levels: 55-79% and 48-87% in control vs. intervention group respectively. Accordingly, these subjects are all high caries risk for future decay and thus will be labeled “high risk” during caries risk assessment evaluation.

When looking at tooth brushing frequency changes it was clear that within both groups there were some noteworthy positive self-reports of increase frequency. This increase in brushing frequency did not correlate with an actual reduction in plaque scores for both groups however. The control group showed an increase of plaque scores, from 45% to 64%, while the intervention group showed a decrease in plaque scores, from 60% to 53%. Snacking frequency on the other hand showed a consistent decreasing trend as both groups had lowered scores at one year compared to baseline, 41% to 39% for the

control group and 52% to 39% for the intervention group. It would appear that even though all children received standard oral hygiene and diet counseling (significantly more in the intervention group), there appears only minimal changes in actual behavior. It was hoped that intensive and more frequent instruction and counseling would dramatically improve these behaviors in this model. One can postulate the children are in fact brushing more frequently, however not as efficiently. In addition, one must take into account that subjects may not be giving accurate behavior histories and reporting only what they think is the “right answer”, as most children often do.

7. Limitations

Having a built in dental clinic in an inner city public elementary school offers many advantages to it’s students, including offering oral health care to low income children who may not have access to dental treatment otherwise. Nonetheless, this system also has limitations, which can create challenging barriers at times. In particular, communication with parents, in regards to their child’s treatment options or oral hygiene instructions, was difficult mainly because the children were not accompanied by their parents- but rather directly pulled from the classroom. Secondly, language barriers, limited phone access or parental location/accessibility were also issues that created obstacles that needed to be worked around. The clinic would often communicate through take home information packets, requiring their signature upon return. Translators were necessary to verbally communicate with many of the parents, many of whom did not speak any English. It was very common for many parents to have more

than one job or even lack a working telephone, making it virtually impossible for them to not only visit the clinic either during or after school hours or even speak on the telephone to discuss treatment or answer any questions they may have regarding their child's oral health. Thus, communication with parents/caregivers was routinely difficult, time-consuming, labor intensive and often lacking in this study.

The recruitment of subjects was another limitation in this school setting due to the above-mentioned reasons. Alternative measures were necessary to in attempts to contact and inform parents or legal guardians of the study. In attempts to recruit patients for the study, indirect promotion through school administrators, teachers, flyers, and take home information were necessary. Rarely was direct parent-researcher contact possible. Researchers often had to rely on multiple attempts from a variety of resources, including waiting for parents out front of the school both before and after school hours, phone calls from translators, staff, researchers and teachers or repeated letters or mailings before obtaining a response. Effective parental-researcher communication was a major hurdle within this study, with issues that may not be encountered at standard community based pediatric dental clinics.

A common issue many oral health care providers face is the overall improvement of oral hygiene behaviors of patients away from the dental office. Verbal/written hygiene instructions along with demonstrations and answering questions are done as efforts in hopes of modifying the habits of patients and tipping the caries balance towards

preventative factors. With any education or efforts geared towards implementing healthy habits, the change ultimately rests on the individual or in this case the parents. These challenges are even more apparent in this study, as the parents are often times not physically present to receive the message personally, and instead must receive this information indirectly through the child either verbally or written. In addition, many of these children did not see their parents on a day to day basis- other family members or caretakers were often a part of the child's every day life.

In hopes of modifying oral health habits towards positive changes, the researchers anticipated that oral hygiene instructions repeated every three months would improve the child's habits at home. While the frequent education has resulted in greater brushing frequency, the plaque scores did not appropriately correlate. As previously mentioned, the data is purely from "self-reported history" from the child subject and may not be reliable or the report is accurate but the quality of brushing is not adequate. Thus, one should keep in mind the possible error of unreliability when analyzing the statistical change within these categories.

Compliance with the xylitol mint therapy was another significant obstacle in this study. The researchers could not monitor nor control how consistent the parents were delivering the mints or if the proper prescribed dose was even given to the subject. As previously noted, xylitol release its maximum benefits and anti-caries effects when a total of 8 gram/day is ingested, split into even and regular intervals. This regimen schedule can be quite challenging for even adults, not to mention young children. It was

particularly difficult delivering the mints to the children in the middle of the day, as the children were at school and had no access to the xylitol, unless provided by the parent in their lunch from home. The researchers collected information regarding the child's pattern of xylitol ingestion through quarterly questionnaires from the parents or self-reports from the child directly. Because the researchers were not able to directly count residual mints during the course of the study, or check the actual amount left over in the bottle, true therapeutic levels could only be assessed through questionnaires and child self-reports. It appears that a six month xylitol mint regimen taken 3-4 times a day will be a challenge for most parents and may be unattainable for more than a brief period of time.

8. Conclusions:

The goal of this study was to address the effectiveness of a modified CAMBRA protocol for 5-9 year-old children. The subjects in the intervention group had better diet modification, more frequent professional fluoride applications, and xylitol product usage based on individual risk status in a 12 month randomized controlled clinical trial at the University of California, San Francisco (UCSF) Tenderloin Elementary School Pediatric Dental Clinic. Our study showed that after one year of xylitol mint therapy and every three-month fluoride varnish placement, there was not a statistically significant decrease in MS, LB and TVC levels at 12 months in the test subjects as compared to the controls. Additionally there was no significant difference between the control and intervention groups when comparing the change of DMFS/dmfs from baseline to one year.

Specifically total tooth surface (tts), decayed surfaces (DS/ds), smooth surface decay (SS-DS/ds) and overall decayed surfaces (DMFS/dmfs) were evaluated.
Caries risk assessment variables had a decrease in plaque and an increase in tooth brushing behaviors, which decreased risk in the intervention group as compared to the controls, but again these differences were not statistically significant.

Although the results this study did not reveal conclusively that a modified CAMBRA protocol for children aged 5-9 statistically reduced cariogenic bacterial counts and caries risk factors, the decrease does show a positive trend in the right direction. Along with lowered MS and LB levels due to the protective properties of xylitol, it is important to note that increased dental visits, oral hygiene information and instructions also play an important role in the frequency of brushing; which leads to better oral hygiene and ultimately promoting the overall prevention of caries. It is also important to point out that the results showed overall xylitol mint at home compliance rates were low and thus a 12 month regimen of 3-4 times per day may not be realistic nor attainable.

A greater number of subjects along with better compliance are necessary to decisively evaluate whether this modified CAMBRA protocol can statistically produce a significant decrease in caries rates within this high caries risk pediatric population. Further studies are also necessary to evaluate the economic, cost-effectiveness and sustainability of such an in-house pediatric dental clinic within an elementary school is an effective delivery system within this population.

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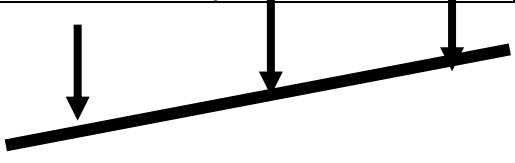
Appendix 1. Caries Risk Assessment Form: Ages 6 Years – Adult

Patient Name: **Subject ID #: RM** **DATE:**
Assessment Date: **Is this (please circle) Baseline or Recall**

Disease Indicators (Any one YES signifies likely "High Risk" and to do a bacteria test)**	**YES = CIRCLE**	**YES = CIRCLE**	**YES= CIRCLE**
Cavities/radiograph to dentin	**YES**		
Approximal enamel lesions (E1, E2) (by radiograph)	**YES**		
White spots on smooth surfaces (Eo)	**YES**		
Restorations last 3 years	**YES**		
Risk Factors (Biological predisposing factors)		**YES**	
MS and LB both medium or high **(by culture**)**		**YES**	
Visible heavy plaque on teeth		**YES**	
Frequent snack (> 3x daily between meals)		**YES**	
Deep pits and fissures		**YES**	
Recreational drug use		**YES**	
Inadequate saliva flow by observation or measurement (**If measured note the flow rate below)		**YES**	
Saliva reducing factors (medications/radiation/systemic)		**YES**	
Exposed roots		**YES**	
Orthodontic appliances		**YES**	
Protective Factors			
Lives/work/school fluoridated community			**YES**
Fluoride toothpaste at least once daily			**YES**
Fluoride toothpaste at least 2x daily			**YES**
Fluoride mouthrinse (0.05% NaF) daily			**YES**
5000 ppm F fluoride toothpaste daily			**YES**
Fluoride varnish in last 6 months			**YES**
Office F topical in last 6 months			**YES**
Chlorhexidine prescribed/used one week each of last 6 months			**YES**
Xylitol gum/lozenges 4x daily last 6 months			**YES**
Calcium and phosphate paste during last 6 months			**YES**
Adequate saliva flow (> 1 ml/min stimulated)			**YES**
****Bacteria/Saliva Test Results: MS: LB: Flow Rate: ml/min. Date:**			



VISUALIZE CARIES BALANCE
(Use circled indicators/factors above)
(EXTREME RISK = HIGH RISK + SEVERE XEROSTOMIA)
CARIES RISK ASSESSMENT (CIRCLE): EXTREME HIGH MODERATE LOW

Doctor signature/#:_____ Date:_____

Appendix 2. Letter to Parent

April 2010

Dear Parent/ Guardian,

Dr. Ling Zhan D.D.S. PhD and Dr. Paul Johnson D.D.S in the Division of Pediatric Dentistry at UCSF School of Dentistry are conducting a study at the Tenderloin Community School's Dental Clinic are looking at better ways to prevent tooth decay (cavities) in children. We are studying if additional anti-cavity (fluoride) treatment, daily use of a sugar-free mints (with a natural sugar substitute, xylitol), and additional dental health information, will help stop future cavities in children aged 6-9 years old. All these treatments will be provided for free if your children participate in the study.

Also, **your children will get paid up to $30 if they complete the study.** If you are interested in having your child participate in this study, please fill the bottom of this form and return it to your child's teacher. Have questions? Call us at **415-614-3005 (UCSF/BAWCC Tenderloin Dental Clinic) on Thursday from 9am-1pm.** We will contact you soon.

Sincerely,
Dr. Ling Zhan/Dr. Paul Johnson

□ **YES**, I am interested in enrolling my child in your study.
□ **No**, I am not interested in having my child participate in your study.

Your child's Name:_____ Class room#:_____
Your name: _____ Contact phone#:_____
Language preferred: _____ Best time to be contacted:_____

The Dental Clinic (located on the lower level of the Tenderloin Community School) is sponsored by
Bay Area Women's & Children's Center & UCSF's Pediatric Dentistry Division

Appendix 3. CAMBRA recommendations form

Recommendations for Control of tooth decay in children over 6yrs old

NAME: _____ Study ID#: RM___/____/____ Date: _____

Daily Oral Hygiene (Aimed at reducing the overall bacteria in the mouth, especially at sites likely to decay. Choose the recommendations based on the danger sites and the conditions of the mouth.)

___ Brush twice daily

___Floss daily

___other:_____

Diet (The most important thing is to reduce the number of between meals sweet snacks that contain carbohydrates, especially sugars. Substitution by snacks rich in protein, such as cheese will also help)

___OK as is

___Limit snacking

___ Limit sodas

___Other: _____

Fluorides (All patients should use fluoride toothpaste twice daily. Additional fluoride products should be added, depending on whether the risk level is medium or high. These fluoride products must be used daily to be effective)

___ Fluoride-containing toothpaste 2x/day (all patients regardless of caries risk status)

___ *Fluoride Rinse (0.05% NaF, ACT or Fluorigard)

*(Use in addition to toothpaste. Patient at medium risk should rinse in the morning or last thing at night. For high risk patients use 2x/day, once in the morning and last thing at night.)

___ 5000ppm Fluoride Gel (Preveident 50000+ or Control Rx "brush –on" daily)

Sugar-free gum/mints

___Chew after meals when you can't brush (xylitol preferred)

___Use Xylitol mints 3-4 times daily

*(recommend for high risk patients, especially those with low saliva flow, and/or those who need to reduce in between meal snacking. The gums or mints that contain xylitol also have an antibacterial effect against the decay-causing bacteria.)

Antibacterial Rinse

___Chlorhexidine Gluconate, 0.12% (Periogard, Peridex, available on prescription).

*(Rinse with 10ml at bedtime for 1 minute, 1x/day for the 1st week of each month)

For patient with dry mouth

___Baking soda toothpaste with fluoride

___Baking soda gum – Dental Vare Gum (Arm&Hammer. It contains baking soda and xylitol) or similar product. Chew frequently throughout the day.

___ Rinse frequently with baking soda suspension during the day (fill sports water bottle with water and add 2 teaspoons of baking soda for each 8oz of water)

Practitioner signature_____ Date_____

Parent/caregiver signature_____ Date_____

Appendix 4. Consent Form

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: Caries Management by Risk Assessment in Children

This is a medical research study. Your study doctor(s), Dr. Ling Zhan DDS PhD, Dr. Paul A. Johnson DDS, or their colleagues from the Division of Pediatric Dentistry, University of California San Francisco will explain this study to you.

The research studies include only people who choose to take part. Take your time to make your decision about participation of your child. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

Your child is being asked to take part in this study because your child is between the ages of 6-9 years old, is currently a patient of the Tenderloin Pediatric Dental Clinic, or is eligible to be a patient in the clinic.

Why is this study being done?

The goal of this study is to investigate if a Caries Management by Risk Assessment (CAMBRA) protocol will prevent new cavities (dental decay) for 6-9 year-old children. The CAMBRA protocol has been well studied and has proved to be effective in reducing cavities in adults. The CAMBRA protocol assesses your child's risk of developing new cavities based on information about their diet, oral care, cavity causing bacterial levels, and current cavity status. If your child is deemed to have a higher cavity risk, the CAMBRA protocol recommends your child receiving more frequent fluoride treatments in the dental clinic, xylitol (a kind of sugar-free sweetener) mints to chew every day at home, and information for you and your child regarding better diet and dental health care. We would like to know if a modified CAMBRA protocol (for children) will be as effective in preventing cavities in 6-9 year-old children as it is in adults.

There will be about 160 children participating in this study.

What will happen if my child takes part in this research study?

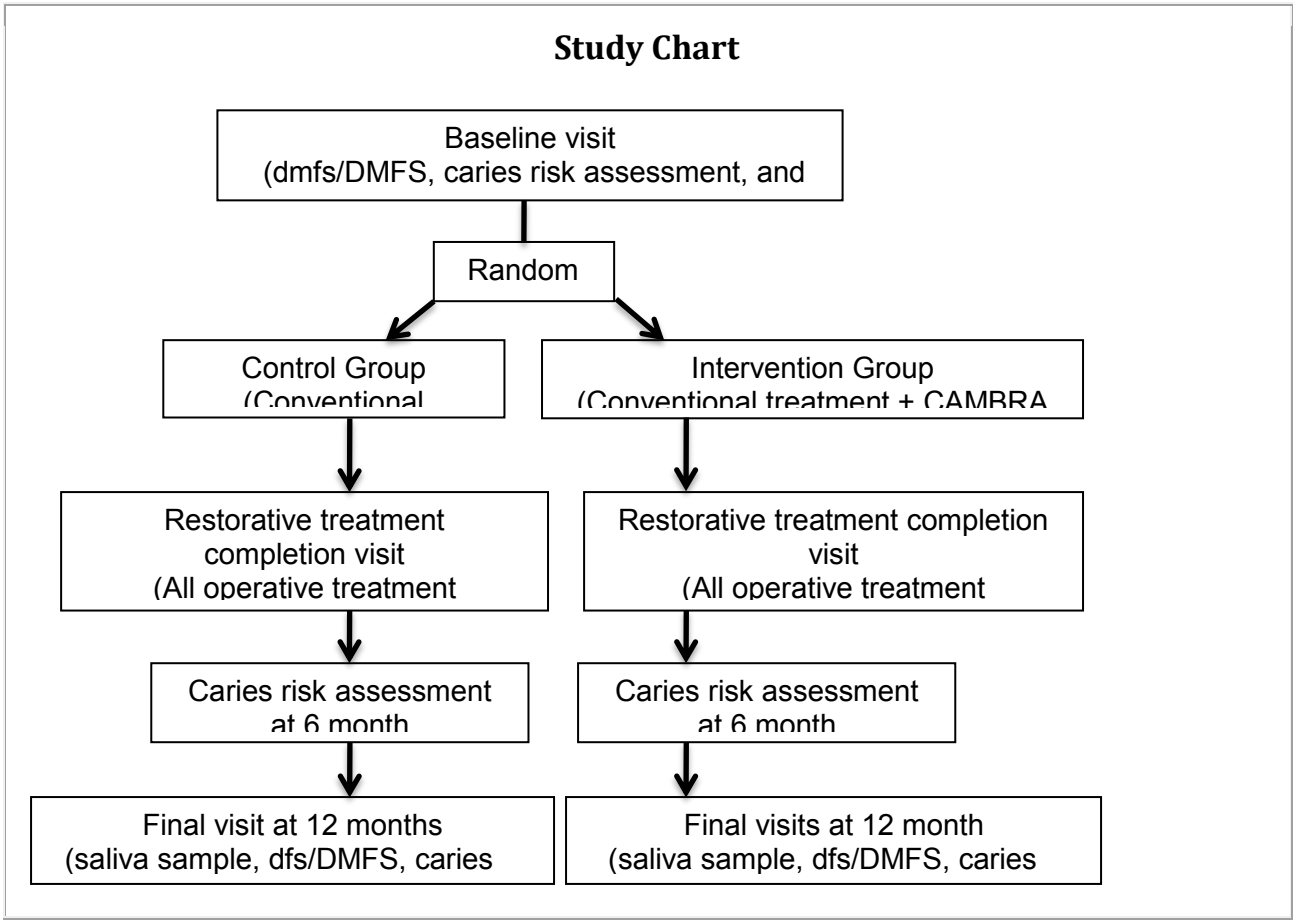
1. At the first visit in the clinic the dentist will look at your child's teeth and record the tooth decay status. You will be asked to fill out a questionnaire about your child. Then your child will chew on a piece of wax for 1 minute and one teaspoon of their spit will be collected in a cup to measure fluoride and cavity causing bacteria levels.

2. Your child will then be randomly assigned to either the control group or the experiment group. Your child will have a 50/50 chance (like flipping a coin) of being placed in one of two groups. Neither you nor your child's doctor will make the choice. This is done so that bias in the study is reduced.
    a. If your child is assigned to the control group
        i. They will continue to receive regular dental care, such as dental restorations and 6 month checkups, cleanings and fluoride therapy, no different then your child's current care.
        ii. At each 6 month checkup and cleaning visit your child will be asked to chew on a piece of wax and spit into a cup to collect saliva to evaluate fluoride and bacterial levels. Risk assessment for tooth decay will be completed at each visit.
    b. If your child is assigned to the experiment group they will receive regular dental care equal to that of the control group, including 6 month checkups, caries risk assessments, fluoride therapy, and collection of spit samples to evaluate cavity causing bacteria and fluoride levels. However, unlike the control group, you and your child will receive additional information on healthy diet, how to keep teeth healthy and a discussion on caries risk status with handouts in person or via phone consultation. Based on your children's risk for new cavities, your child will get the following additional treatment:
        i. **High risk**: two xylitol mints 3-4 times daily, every 3 month fluoride varnish applications
        ii. **Moderate risk**: two xylitol mints 3-4 times daily
        iii. **Low risk**: No additional treatment

        As part of the study, your child will be required to bring home a one page questionnaire consisting of five questions once every month, which you will need to fill out and return promptly. The goal of the monthly questionnaire is to help the researchers to assess how well the home care regimens are being followed, to assess if there have been any side effects from the treatments and to answer any questions or concerns that you may have. If the questionnaire is not filled out and returned, you will be contacted by the study supervisor.

3. After one year the study will be finished. A final exam will be completed and your child will again be asked to spit into a cup after chewing wax for one minute.

The following chart descries the outline of the study.



How long will my child be in the study?

Participation in the study will take a total of about one (1) year. You will be asked at the end of the consent if you are interested in being contacted if we have future studies.

Can my child stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can my child expect from being in the study?

Your child may have side effects during the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors cannot predict all the side effects that may happen.

Side effects (if any) may be mild. You should talk to your study doctor about any side effects your child experiences while taking part in the study.

Side effects of the standard dental care including regular dental check-ups, dental cleaning, fluoride varnish treatment, and restorative dental treatment are the same as your child would get from his/her regular dentist.

Risks and side effects related to the *Xylitol mints* treatment may include:

- Flatulence (gas)
- Soft stool or diarrhea

Each xylitol mint contains 0.5 g of xylitol. The maximum intake of xylitol per day will be less than 8g in the current study. The most common side effect documented by the reporters was gas and soft stool or diarrhea when intake is over 45g daily. These levels are much greater than the amount needed to have dental benefit, which is 6-8g/day. Xylitol is an FDA approved food additive sugar substitute. The short- and long-term human studies which have showed a favorable safety history of consumption of xylitol in controlled studies by human volunteers, as well as by the public at large, have not been associated with any significant adverse effects. The consumption of xylitol has a long history of safety. The Turku sugar studies from 1975 provided evidence that adults who consumed very high levels of xylitol per day (average of 53 grams) over two years did not show any adverse effects.

Fluoride varnish efficacy in primary teeth was evaluated by Dr. Jane Weintraub in 2006. Her clinical study on fluoride varnish showed significant cavity reduction in her study population with no related adverse events reported. The American Academy of Pediatric Dentistry advocates professionally applied topical fluoride due to its well studied cavity reduction effects with negligible adverse events.

- **Randomization risks:** You will be assigned to a treatment program by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other study group.

- **Unknown Risks:** The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

- For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your child's health better. While doctors hope these additional interventions will be more effective than the standard treatment regimens, there is no proof of this yet.

If your child is in the group that receives additional information, more frequent checkups and fluoride, as well as xylitol mints and it proves to reduce dental caries more effective than standard therapy, your child may benefit from participating in the study, but this cannot be guaranteed.

There may be no direct benefit to your child from participating in this study. However, this study will help doctors learn more about intervention, and it is hoped that this information will help protect all children from dental decay and infection.

What other choices do I have if I do not want my child to take part in this study?

Your other choices may include:

- Getting no treatment
- Getting standard treatment for your condition without being in a study.
- Getting a different experimental treatment/taking part in another study.

Please talk to your doctor about your choices before deciding if you will take part in this study.

Will my child's medical information be kept private?

Yes. No personal information will be shared. Only the study investigator will have access to your child's records as it pertains to the study. Participation in research may involve a loss of privacy; however, the research records will be handled confidentially. All records will be coded, and kept in locked files so that only the study investigators have access to them. No individual identities will be used in any reports or publications resulting from this study. All laboratory samples and records will be identified by the unique subject code only without subject's identification information. No identifiable/coded study data will be shared with the sponsoring individual/institution.

What are the costs of taking part in this study?

You will not be charged for any of the study activities.

The costs of all standard dental visits and treatments described above will be billed to you or your insurance carrier or Funds that ran the Tenderloin Pediatric Dental Clinic, with the exception of *extra fluoride, xylitol mints, information packets, tooth brushes/floss etc.,* which will be paid for by the study.

Will I or my child be paid for taking part in this study?

You or your child will be paid $10 at each visit: the baseline, 6 month, and 1 year follow-up. In return for your time, effort and travel expenses, your child will receive additional dental checkups, additional oral health information, extra fluoride treatment, xylitol mints, tooth brushes/floss along with the $10 per visit.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Dr. Ling Zhan or Dr. Paul Johnson, if you feel that your child has been injured because of taking part in this study. You can tell the doctor in person or call him/her at 415-476-3276.

> **Treatment and Compensation for Injury:** If you are injured as a result of being in this study, treatment will be available. The costs of the treatment may be covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide not to take part in this study, you may withdraw your child from the study at any time. No matter what decision you make, there will be no penalty to you or your child, and your child will not lose any of their regular benefits. Leaving the study will not affect your child's medical/dental care. You can still get your child's medical/dental care from our institution.

We will tell you about new information or changes in the study that may affect your child's health or your willingness to continue in the study.

In the case of injury resulting from this study, your child does not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctor(s) Dr. Ling Zhan or Dr. Paul Johnson at 415-476-3276.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at 415-476-1814

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

Are you interested in being contacted for future studies? ☐ Yes ☐ No

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent

The person being considered for this study is unable to consent for himself/herself because he/she is a minor. By signing below, you are giving your permission for your child to be included in this study.

Date	Parent or Legal Guardian

Appendix 5. CHR Approval Form

COMMITTEE ON HUMAN RESEARCH
OFFICE OF RESEARCH, Box 0962
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
www.research.ucsf.edu/chr/Apply/chrApprovalCond.asp
chr@ucsf.edu
(415) 476-1814

CHR APPROVAL LETTER

TO: Ling Zhan, Ph.D., D.D.S. Box 0758
John D.B. Featherstone, M.Sc., Ph.D. Box 0430,

RE: Caries Management by Risk Assessment in Children

The Committee on Human Research (CHR) has reviewed and approved this application to involve humans as research subjects. This included a review of all documents attached to the original copy of this letter.

Specifically, the review included but was not limited to the following documents:
Specimen Consent Form, Dated 4/1/2010
Parental Permission Consent Form, Dated 4/1/2010
Assent Form, Dated 4/1/2010

The CHR is the Institutional Review Board (IRB) for UCSF and its affiliates. UCSF holds Office of Human Research Protections Federalwide Assurance number FWA00000068. See the CHR website for a list of other applicable FWA's.

APPROVAL NUMBER: H11691-35389-01. This number is a UCSF CHR number and should be used on all correspondence, consent forms and patient charts as appropriate.

APPROVAL DATE: April 5, 2010 **EXPIRATION DATE:** March 16, 2011 **Full Committee Review**

GENERAL CONDITIONS OF APPROVAL: Please refer to www.research.ucsf.edu/chr/Apply/chrApprovalCond.asp for a description of the general conditions of CHR approval. In particular, the study must be renewed by the expiration date if work is to continue. Also, prior CHR approval is required before implementing any changes in the consent documents or any changes in the protocol unless those changes are required urgently for the safety of the subjects.

HIPAA "Privacy Rule" (45CFR164): This study does not involve access to, or creation or disclosure of Protected Health Information (PHI).

Sincerely,

Reese T. Jones, M.D.
Chair, Committee on Human Research

cc: Paul Johnson, Box 0753

Appendix 6. Parent Quarterly Mint Questionnaire

UCSF-Tenderloin Community School Dental Clinic
Parent's Quarterly Questionnaire
for CARIES MANAGAMENT BY RISK ASSESSMENT IN CHILDREN STUDY

Please fill out and return the form to us. If you have any questions or concerns about the study, please call Dr. Johnson or Dr. Zhan at **415-476-3276**.

Please circle the best answer for each question listed below:

1. **How many xylitol Tablets are you giving your child per day?**
    a. Less than 2 Tablet per day
    b. 2 Tablets 2 times per day
    c. 2 Tablets 3 time per day
    d. 2 Tablets 4 times per day
    e. More than 2 Tablets 4 times per day

2. **Approximately, how full or empty is the bottle of xylitol mints as of today?**
    a. Less than one-quarter (1/4) of a bottle
    b. Less than one-half (1/2) of a bottle
    c. Greater than one-half (1/2) of a bottle
    d. Greater than three-quarters (3/4) of a bottle
    e. Bottle is empty

3. **Have you or your child noticed any problems since your child started the study?**

    a. Yes b. No

    If **YES**, please circle
    1. gas
    2. nausea, upset stomach, or vomiting
    3. diarrhea
    4. other: _____

4. **Are you able to give your child xylitol mints for 3-4 times daily?**

    a. Yes b. No

    If **NO**, please explain:

5. **Do you have any questions or concerns about the study and would like to talk to us?**

a. Yes b. No

If **YES**, when is a good time to call?
Day/time _____ Best phone number: _____

Thank you,

Dr. Johnson & Dr. Zhan

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Author Signature

6/10/14

Date