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Caries Management by Risk Assessment in Children

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Caries Management by Risk Assessment in Children

Paul Aaron Johnson

Abstract

Purpose: To investigate the efficacy of a modified caries management by risk assessment (CAMBRA) protocol on reducing the cariogenic bacterial load, improving oral hygiene care and dietary habits on children aged 5-9 years old.

Methods: Sixty-six children aged 5-9 years old participated in a single blind randomized controlled clinical trial and were assigned to either the modified CAMBRA or regular treatment group. Parents of intervention group were asked to give child 6-8g of xylitol mints per day (8-12 mints/day) for a total of six months. These individuals were seen every 3 months for fluoride varnish application, oral hygiene and diet evaluation with counseling. Additional diet and oral hygiene information was sent home to parents. dmfs/DMFS scores, caries risk assessment, saliva samples were taken at baseline and at 6 months and MS, LB and TVC of bacterial levels tabulated.

Results: MS, LB and TVC at baseline and 6 month showed slight decrease but there was no statistical significance between the modified CAMBRA and regular treatment groups $p<0.05$. There was consistent trend of decreasing caries risk factors (tooth brush and snacking frequency, plaque scores) from baseline to 6 months however these changes between the two groups were not statistically significant as well.

Conclusion: 6-8g of daily xylitol mints showed a minimal, but not statistically significant decrease in cariogenic bacterial load in the oral cavity. Increased frequency of professional oral hygiene and diet counseling shows a positive trend in decreasing caries risk behavior at six months in this population.

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1. Introduction

The Surgeon General's 2000 US Public Health Report finds dental caries is the single most common chronic childhood disease in the United States and among 5- to 17-year-olds, dental caries is more than 5 times as common as a reported history of asthma and 7 times as common as hay fever.[1] Despite the reduction in dental caries in recent years, more than half of all children have caries by the second grade, and by the time students finish high school, about 80 percent experience caries.[2] On average, 3.1 days of school were lost per year due to dental pain or infection.

It is also known that children of low-income families suffer the highest number of caries and oral pathology.[3] Caries seen in these individuals is more likely to be untreated than caries in those living above the poverty level; more than one third (36.8 percent) of poor children aged 2 to 9 have one or more untreated decayed primary teeth, compared to 17.3 percent of non-poor children. Untreated diseases, pain and infection can lead to problems in eating, speaking, and learning.[3]

Dental caries continues to be a major problem in children and adolescents in the US. The impact on society of oral diseases in children is substantial. It has been estimated that the annual cost of dental caries treatment in children accounts for as least $4.5 billion in the US.[1]

2. Background and Significance

Dental Caries and the Caries Balance

Dental caries is an infectious disease. At this time, the disease process itself has been extensively studied and is well understood.[4, 5] It is known that the main bacterial species responsible for enamel demineralization and lesion progression are Mutans streptococci (MS) and lactobacilli (LB). Studies have 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. They also produce glycoamino-glucans which allow them to adhere tightly a tooth's surface. If these bacterial colonies are left unperturbed on the tooth's surface, a localized drop in pH will occurs when fermentable carbohydrates are present, acid production increases and a dissolution of the enamel carbonated hydroxyapatite structure progresses. Extensive demineralization of the tooth's enamel weakens the structure leaving it more vulnerable to future acid attack. Continuous acid challenge will eventually cause cavitation and irreversible damage to the tooth structure.[4, 5]

Studies have shown 6-9 year-old age groups show the highest risk for dental caries in mixed dentition, thus increasing caries risk for early permanent dentition during adolescence.[7] The NHANES III study 1999-2002 show the prevalence of dental caries was 49.0% and 20.1% in deciduous and permanent teeth respectively among 6-11 year-

old children, while the caries prevalence among 12-15 year-old adolescents was 49.6% in permanent teeth.[8] This data highlights the seriousness of caries of the primary dentition and direct connection to caries in the permanent dentition.

Lastly, in vivo human studies have shown that higher levels of MS and LB in saliva or plaque are associated with higher caries rates.[7, 9, 10] And, contrary to popular belief, studies continue to find that placement of dental restorations has only minimal effect on the overall cariogenic bacterial levels in the mouth.[11]

Caries Prevention

Diet

The role of sugars and fermentable carbohydrates are known risk factors in the development of caries. Common food items found in the diet of U.S. children which contain high levels of these items are: fruit juices, sodas, chips, crackers, cookies and fast food items.[12, 13] During, and for a up to an hour after ingestion of items containing these substances, pH levels drop due to their metabolism by MS and LB and resultant production of lactic acids.[4, 14] Stephan et. al. has shown the initial pH drop following sucrose ingestion is quite rapid with the lowest pH being attained within a very few minutes. However, pH recovery has been shown to take between fifteen to forty minutes depending to a large extent on the acid buffering properties and clearance

properties of the individual's saliva.[15] The initial rapid drop in pH is due to the ease of these bacterial species s to metabolize sucrose. Larger carbohydrates, such as starch, diffuse into plaque more slowly and have to be broken down before bacterial metabolism can take place. This delay contributes to sustained and delayed low level acid production after ingestion.

Enamel dissolution begins when plaque pH is reduced to levels between 5 and 6, and is thus called the “critical value”. The period of critically lowered pH needed for caries to occur is mainly a function of the type and frequency of the carbohydrates consumed as well as the microbial composition of the tooth biofilm and salivary factors. Repeated and prolonged daily ingestion (i.e. snacking) of high sugar or fermentable carbohydrates allows for sustained reduction of pH levels within the critical value and a net loss of tooth mineral. Repeated exposure over a period of time ultimately leads to caries formation, cavitation and irreversible tooth structure damage.[4]

Similar to caries development, excess consumption of carbohydrates, fats, and sodium have been shown to contribute to poor systemic health, including malnutrition and obesity.[16] In an effort to educate health providers and the general public regarding healthy dietary choices, the U.S. Dept. of Agriculture along with the Dept. of Health and Human Services produce and distribute extensive dietary guidelines and information, and have done so annually since the 1960’s.[17] Oral and health care professionals have long endorsed healthy food choices armed with the knowledge that high sugar and carbohydrate diets lead to a number of chronic diseases, including dental caries.[18]

Dietary intake is ultimately up to the individual, however it is the oral health care provider's obligation to inform and educate their patients regarding healthy lifestyle choices and the risks and possible outcomes if ignored.[19]

Dietary guidelines for both the dental provider and the patient aimed at caries prevention have been established by the American Dental Association as well the American Academy of Pediatric Dentistry. These guidelines are backed by studies which show clearly that with proper and reasonable dietary modification which include healthy foods along with reduction of the frequency and duration of high sugar or carbohydrate diets, a reduction of caries incidence is noted.[20-27] The guidelines include recommendations such as: Eat a balanced diet rich in whole grains, fruit and vegetables, and practice good oral hygiene. Eat a combination of foods to reduce the risk of caries and erosion; include dairy products with fermentable carbohydrates and other sugars and consume these foods together, not as individual snacks. Add raw fruit or vegetables to meals to increase salivary flow. Choose water over acidic or sugar laden beverages. Rinse mouth with water regularly and chew sugarless gum to wash away food debris and stimulate saliva. Avoid frequent snacks to reduce repeated exposure to sugars, other fermentable carbohydrates and acids.

Educating the child and parent on proper diet and oral hygiene practices with the hope such information will positively influence future behavior is a primary goal of any preventative regimen. A general conclusion from three systematic reviews regarding oral health promotion activities concluded that individual knowledge about oral health can be

improved and that health promotion programs that increase knowledge may also change behaviors, but the author cautioned, that the causal relationship between knowledge and subsequent behavior is minimal.[28] To maximize success in a individual making positive dietary changes, advice for dental health should be personal and positive and should be in line with dietary advice for overall systemic health.[29] In combination with aggressive preventative regimens including antimicrobial therapy, fluoride therapy, oral hygiene and diet counseling have been shown to significantly reduce the new caries incidence in a high risk adult population.[28]

Sealants

The use of protective resin-based dental sealants on permanent molars has been shown to significantly reduce caries incidence on pit and fissured surfaces.[30] Caries reduction rates for these surfaces in children and adolescence have been shown to be as high as 86 percent at one year and 65 percent 9 years following placement.[30, 31] With routine follow up and monitoring, these types of pit and fissure sealants have been shown to be a cost effective and (relatively) simple method of reducing caries in this population.

Although resin-based sealant usage on children and adolescence has shown steady increase since their introduction in the 1980's, the latest data from U.S. Department of Health and Human Services initiative Healthy People 2010 shows they are still underutilized with only 50 percent of this population having received sealants on

permanent molars.[32] For the health care professional, resin based sealants are an underutilized, effective tool in the preventative dentistry arsenal.

Fluoride

The use of fluoride as an anti-caries protective treatment has been in use in the United States since the 1960's. Many methods of fluoride delivery are routinely used, such as in dentifrices, rinses, gels and through the public water supply. One fairly novel method of fluoride delivery is the use of a varnish carrier. Although it has been a viable dental product for forty years as a "desensitizer", and early studies showed significant caries reduction since the 1960's,[26, 33] it has only been recently embraced as a topical medicament solely for caries prevention.

Fluoride varnishes were first introduced in Europe in 1960's as a topical fluoride for patients with sensitive teeth, but has most recently been used off-label as an anti-cavity treatment in adults and children. Duraphat was the first varnish to be marketed for this purpose. Currently there are over ten manufacturers with similar products being sold in Europe and the United States.[34] In 1997 the FDA approved fluoride varnish use as a cavity liner and desensitizer. It has been approved as Class II Medical Device for use as a cavity liner and/or tooth desensitizer. Currently no fluoride varnishes products are FDA approved as caries preventive agents [35] and any use other than a "desentizier" is

considered “off label useage” although much research has come forth recently supporting varnish as an effective caries prevention agent.[36]

Fluoride varnishes comes in 1%-5% Sodium Fluoride and Difluorsilane concentrations in a resin or polyurethane base. Upon application to the tooth surface the varnish solidifies then hardens when it comes in contact with saliva. Once hardened it releases fluoride ions directly into the saliva and enamel surface where remineralization takes place. This direct adherence to tooth surface allows for prolonged (1 – 7 days) fluoride release while minimizing excess systemic ingestion.

Recent studies have shown a 18.3% reduction in DMFS scores for children when professionally applied at six month intervals.[37] The use of varnish is considered "off label" for caries prevention,[36] however numerous current studies have shown fluoride varnish efficacy with caries reduction in children,[33, 34, 38-42] and it’s use has been adopted and recommended by the American Dental Association and the American Academy of Pediatric Dentistry for use in caries reduction. Fluoride varnishes have been approved as a Class II Medical Device for use as a cavity liner and/or tooth desensitizer by the U.S. Food and Drug Administration.[35]

Varnish has many advantages over other topical applications; has a rapid, simple delivery method, minimal fluoride ingestion, low cost and prolonged duration of fluoride release at the site(s) of interest. From a public health standpoint, fluoride varnish is looked at as a

practical and cost effective instrument in delivering fluoride to high caries risk populations, in particular, the primary dentition of children.[43-45]

Chlorhexidine

Chlorhexidine gluconate mouth rinse is a chemical antiseptic with bactericidal and bacteriostatic actions on both gram-positive and negative bacterial species. It has been shown to 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.[46] Chlorhexidine has both immediate and prolonged effect on these oral bacterial species by binding and absorbing into the tooth pellicle.[47] Both invitro and in vivo studies have shown chlorhexidine ability to disrupt plaque formation and alter concentrations of MS. It's particularly effective when combined with fluoride therapy.[48]

Although Chlorhexidine has been approved by the FDA and has been shown to be safe with no serious negative side effects, it's continual use has been reported to cause extrinsic tooth staining, and it's taste to be displeasing by it's users. Lastly, it is logical to assume that lower levels of MS and LB levels should directly equate with a concomitant lower risk for future caries, and this very well may be true. However, this supposition has little scientific backing at present and further studies are needed to substantiate this proposed relationship.[48-50]

Historically, with regards to chlorhexidine use, children have shown an adversity to its bitter, metallic taste. Due to concerns over compliance, it is not routinely utilized in this population as part of a long term, daily at home antimicrobial regimen for children.

Xylitol

With the clear understanding of the microbial caries process, locating dietary sugar substitutes which do not promote dental decay has been a critical point of interest in cariology research for decades. Many sugars have been evaluated, and one group has stood out, namely the sugar alcohols, or polyols. Polyols such as sorbitol, mannitol, and xylitol have been shown to be non-cariogenic and do not promote tooth decay.[51] Aciduric and acidgenic oral bacteria such as MS and LB cannot metabolize these structures, and consequentially do not produce acids**.**

Xylitol in particular appears to have the greatest cariostatic effect.[52-55] Xylitol is well tolerated by adults as well as children, and comes with minimal to no side effects.[22, 53, 56] Because xylitol cannot be metabolized by MS, it competes with sucrose in the intra-cellular metabolism process, thus reducing the energy source required for reproduction and acid production.[57] Short-term xylitol consumption has been shown to decrease 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.[54, 55]

Human consumption of xylitol has a long history. Xylitol is produced from Xylan, which is found in multiple hardwood species, explicitly the birch tree. Xylan is also found in lesser quantities in some fruits and vegetables. This sugar precursor is processed and refined in a similar manner as sucrose, however, due to its more labor intensive process and lesser industrial infrastructure, xylitol end cost is much higher than that of sugarcane or corn sugars to produce.[58]

Xylitol was approved by the Food and Drug Administration (FDA) in the 1960's and is considered safe for children as a direct food additive for use in foods for special dietary uses.[59] One of the major studies looking at xylitol safety was the adult Turku sugar studies conducted in 1975-76.[56] Volunteers consumed xylitol orally (an average of 53 grams/day) for two years. The results of the study showed no negative or adverse reactions for the duration of the study. The study also looked at biochemical, carbohydrate, and energy metabolism, and found no differences from controls. 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.[60]

Research has shown that xylitol has a protective effect and inhibits tooth decay.[54, 61, 62] In 1998 American Dental Association backed the use of polyols, including xylitol, if used as part of a comprehensive oral hygiene program to promote oral health. Extensive research conducted over the last two decades looking at dose response to xylitol has lead

to recommendations for ideal dose/therapeutic range. To gain the desired reduction in MS and levels, one must consume between 6.44g to 10.32g of xylitol (per day).[63] Between this dose range a plateau effect was noted and ideal reduction of MS levels were found.[63] If taken daily within this range, MS reductions will be noted as early as five weeks in plaque and up to six months in both plaque and unstimulated saliva. It is also clear there is a linear response between xylitol ingestion frequency and MS reduction.[64] This reveals that for xylitol to be effective in reducing MS levels, not only must the dosage stay within optimum levels, but also must maintain optimum frequency of ingestion, which is a minimum of three times per day.

Xylitol products have shown good acceptance in children and demonstrated great potential for caries prevention through modification of oral flora composition. Most studies utilize gum as the xylitol delivery systems and have seen marked reduction of MS counts when xylitol distribution has been tightly monitored.[63] In another study, significant reductions in *MS and SS* levels were observed after six weeks of gummy bear snack consumption containing xylitol at 11.7 or 15.6 gram per day divided in three exposures. These results suggest that a xylitol gummy bear snack may be an alternative to xylitol chewing gum for dental caries prevention.[52]

There has been some concern of the saliva stimulation effect and mechanical dislodging action of chewing gum which may falsely overestimate the MS bacterial reduction capability of xylitol. However, the use of oral xylitol syrup administered topically two or

three times each day at a total dose of 8 grams has also been shown to be effective in preventing Early Childhood Caries as well.[53]

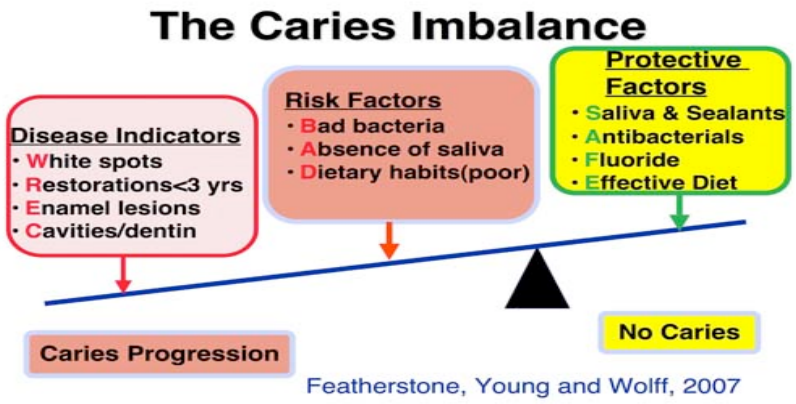
Utilizing yet another delivery method for xylitol, in a recent study, 44 mother-infant pairs participated in a double-blinded randomized controlled clinical trial to assess the efficacy of the three times daily use of xylitol wipes in 6-35 month-old children with high caries risk. Mothers were instructed 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 (unpublished data). The data also indicated that MS genotypes were less likely to be retained in the xylitol group, suggesting that xylitol modifies MS colonization.[65]

Due to patient taste acceptance, positive anti-caries benefits, along with marketability of said items with xylitol, some United States manufactures of items such as gum and mints have been incorporating xylitol into their products. Unfortunately, most likely due to expense, the small quantity of xylitol in these items have little clinical benefit. However, as the public becomes more aware of the positive benefits of xylitol, we can imagine these companies will most likely adapt to the demands of the market and will start producing items with clinically beneficial amounts of xylitol in the coming years.

Caries Management By Risk Assessment

At present, many recent studies have demonstrated that caries progression, or reversal, is a delicate balance between many factors, namely, bacterially generated acid challenge 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, 14] (Figure 1).

Figure 1 Caries Balance



To counter or break the caries cycle, risk factors that tip the balance toward caries progression must be countered by protective factors. These protective factors include the reduction of cariogenic bacteria by antibacterial treatment, enhanced remineralization by fluoride, and increased 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, 14, 24]

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).[11, 48]

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). Once a risk level has been assigned the practitioner can then use the CAMBRA Clinical Guidelines chart (Figure 3) to help determine the best tools to use for optimum caries management.

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, 11, 14, 24] It also increased the percent of patients with few or no new caries.

These findings confirm that caries risk assessment coupled with therapeutic interventions reduced the need for caries restorative treatment compared with conventional restorative dental treatment in an adult population. Caries management by risk assessment (CAMBRA) guidelines have been shown to significantly reduce dental caries (cavities) increments as compared to conventional caries care in adults aged 18 years and older.[11] However, as of yet, these same results have not been proven in children.

Treatment Modalities in Children:

Studies have shown that caries in the primary dentition is a predictor for caries in the permanent dentition.[7] 6-9 years old is a very critical age group with the start of the emergence of permanent teeth and the peak development of caries in primary dentition. This is also an important time in a child's life as they develop appropriate dietary and oral hygiene habits. 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 employ the use of chlorhexidine and/or high concentration fluoride toothpaste (5,000 ppm F) home treatments. Historically, use of chlorhexidine mouth rinses to control MS infections in children is not frequent because of dissatisfaction with taste and thus concern over compliance. In general, high concentration fluoride toothpaste is also not recommended for children due to the risk of fluorosis in developing permanent incisors and first molars from accidental over-ingestion.

If antimicrobial treatments such as xylitol products are accepted and used by patients, their oral microbial flora composition can be modified. It then may be possible to 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.[66, 67] However, no study has been conducted to validate the efficacy of this regimen in children. Thus, studies are needed to evaluate this paradigm of caries risk assessment and caries management methods in children between the ages of 6-9.

Aims, Significance, and Hypothesis

The overall aim of this study is to provide clinical evidence that the use of scientifically based caries risk assessment tool (CRA) in conjunction with aggressive preventive and therapeutic measures to restore the balance between pathological and protective factors, together with conservative restorations will result in reduction of cariogenic bacterial load (MS & LB) and caries risk of subjects compared to control treatment. Specifically, we hope to determine the efficacy of CAMBRA in reducing MS & LB levels in 5-9 year-old children in a unique elementary school dental clinic setting as well as modifying the oral hygiene and dietary habits of these subjects. 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

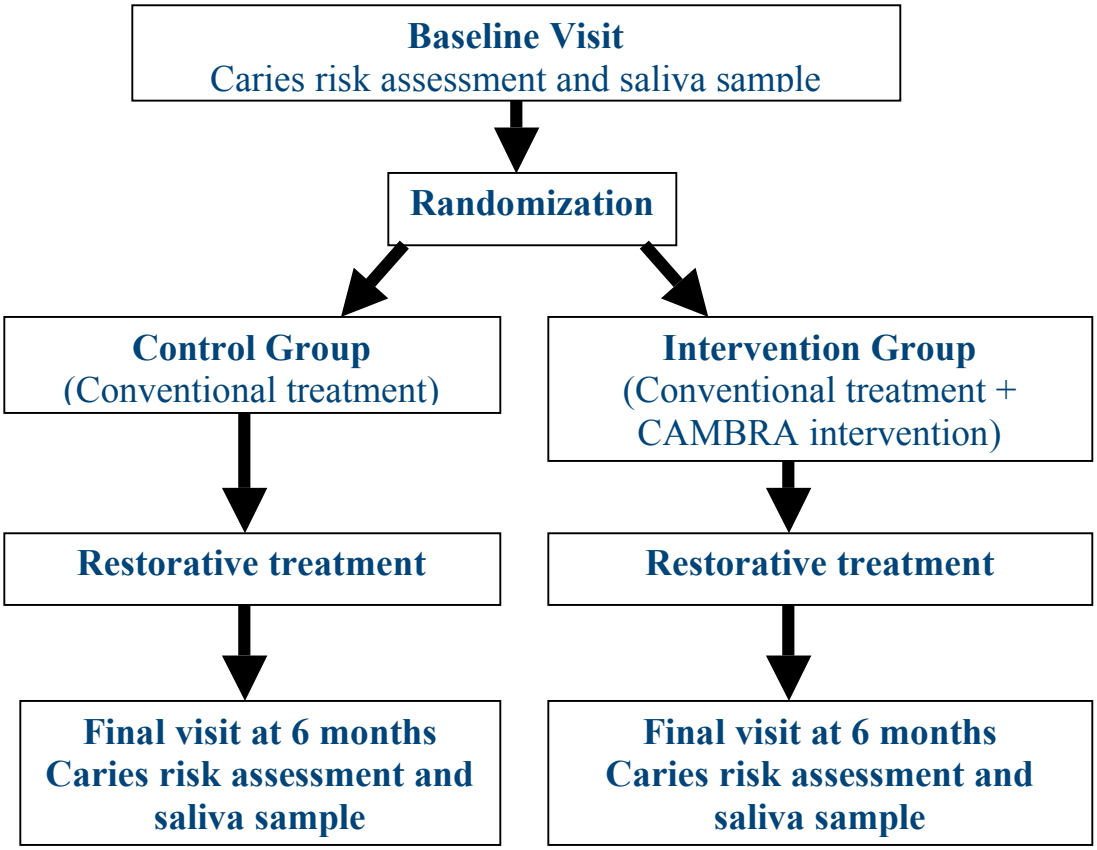
dietary and oral hygiene habits with a concurrent short-term and long term decrease in future caries prevalence within this population.

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



Sample size calculation was based on similar studies which measured mutans streptococci levels with xylitol use in children.[63] A total of 60 subjects were needed at power β=0.80 with a two-sided type I error α at 0.05 and 15% drop out rate. A total of 68 subjects ages 5 to 9 years old who attended the Tenderloin Community Elementary School and Dental Clinic between April 2010 to June 2011 were recruited into the study after meeting eligibility requirements.

Inclusion criteria required that subjects could participate if they were to maintain 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 had prolonged antibiotic use in the past three months or dental needs outside of the community pediatric clinics, such as care which would require treatment in specialty clinics.

Drs. Zhan or Johnson 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 wereplaced 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" refers to subject with no disease factors and minimal risk factors that are well balanced with protective factors. "Moderate Caries risk" refers to individuals without any of the disease indicators, but with predominance for risk factors in combination with minimal utilization of protective factors. Medium risk is thus more arbitrary and limited to clinician subjective expertise.

Caries risk status was not made known to either the study participants or the dental care providers until the end of the study. 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.

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.

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.[68] 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.

4. Results

Subject Demographics at Baseline

A total of 65 children aged 5-9 years (mean age 6.88 +/- 1.55 years) were recruited for the study with thirty-four females and thirty-one males. The baseline demographics are summarized in Table 1.The predominate race/ethnicities of study subjects were Hispanic (39%) and Asian (24%), followed by white/other (14%), African American (11%), and Native American/Pacific Islander (9%). There were eight pairs, and one triplet of siblings recruited in the study. 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 and diet information. The intervention group and control group had no significant difference in age, gender, bacterial level and other clinical variables at baseline but had significantly difference in race/ethnicity (P = 0.045).

Table 1. Baseline Demographics

	Control Group		**Intervention Group**	
	n	**Mean ± SD**	**n**	**Mean ± SD**
Age	28	6.89 ± 1.45	34	6.88 ± 1.65
Gender : Female (%)	28	15 (53.57%)	35	18 (51.43%)
Race/Ethnicity (H/AA/NA/A/O)*	28	8/4/6/5/5	33	16/3/0/10/4

* H: Hispanic; AA: Africa Americans; NA: Native Americans; A: Asian; and O: Other.

Baseline decayed, missing and filled surface (DMFS/dmfs) data for both permanent and primary dentition were collected from each subject and will be compared at one year (ongoing study). Between the two groups, there were no statistical differences at baseline with number of teeth (# Teeth), decayed surfaces (DS), smooth surface decay (SS-DS), smooth surface DMFS (SS-DMFS) or overall decayed, missing of filled surfaces at baseline (P>0.05) as presented in Table 2.

Table 2. Baseline Caries Data

	Control (N=30)	**Intervention (N=32)**
	Mean ± SD	**Mean ± SD**
# Teeth	22.10 ± 1.97	21.5 ± 3.29
DS	8.43 ± 11.10	8.97 ± 10.07
SS-DS	5.10 ± 7.15	4.44 ± 5.96
SS_DMFS	8.53 ± 9.29	6.63 ± 7.74
DMFS	15.37 ± 13.98	15.03 ± 13.55

Attrition, Compliance and Adverse events

For the duration of the study, all subjects met the study inclusion criteria and were concurrently enrolled in both the Tenderloin Community Elementary School and affiliated UCSF/BAWCC on-site Dental Clinic. Three subjects dropped due to

relocation/school transfer, and three subjects were unable to be located (school absence) during the week of their final six-month exam and saliva collection, revealing a 9.2% dropout rate.

Xylitol mint at-home compliance was measured by take home parental questionnaires at three and six months. Two subjects (one sibling pair) refused to take the mints three months into the study. At the three month evaluation, 58% of parents reported they were able to give equal or greater than 12 mints per day to their child as prescribed. Most parents reported difficulty in giving the child mints more than two times per day, morning and night) and the remainder of these parents reported they were giving the child less than three mints per day even when contacted by the study supervisor and instructions regarding mint quantity and frequency were reviewed. By six months the mint compliance rates dropped to 41% as shown in table 3. There were no aversive events reported associated with either fluoride or xylitol therapy aside from the sibling pair that didn't like the taste of the mints.

Table 3. Xylitol Mint Compliance

n = 30	Questionnaires' Reviewed	% children given < 8 mints/day (under therapeutic dosage)	% children given >/= 12 mints/day (therapeutic dosage)
3 months	24	42	58
6 months	17	59	41

All subjects were healthy and able to complete comprehensive restorative dental treatment at clinic before completion of study.

Bacterial levels in baseline and 6 months

Baseline bacterial levels showed no statistical differences in logMS, logLB or logTVC ($P>0.05$) between the two groups although logMS in the intervention was slightly higher than that of Controls. The bacteria levels of both groups at baseline and 6 month are summarized in Table 4.

There were minimal changes on bacterial levels on log MS, logLB and logTVC in both groups (see Table 4). All bacterial levels at 6 months were not significantly different between intervention and control groups (all the P values > 0.05) and were not significantly different from baseline within each group (all the P values > 0.05).

Table 4. Bacterial levels at baseline, 6 month visits, and change of bacterial levels in the two groups

	Control Group		**Intervention Group**	
	Baseline Mean ± SD (n=30)	**6 months** Mean ± SD (n=27)	**Baseline** Mean ± SD (n=35)	**6 months** Mean ± SD (n=30)
Log MS	3.99 ± 2.21	3.80 ± 2.08	4.46 ± 1.99	4.07 ± 2.01
Log LB	1.84 ± 2.36	1.56 ± 2.09	1.82 ± 2.27	1.46 ± 2.08
Log TVC	8.46 ± 0.27	7.61 ± 2.76	8.48 ± 0.32	8.24 ± 1.59
Change of bacterial levels			**P Value for group difference**	
	Control (n=27)	**Intervention (n=30)**		
	Mean ± SD	**Mean ± SD**		
Log MS	0.01 ± 2.59	-0.19 ± 2.44	0.78	
Log LB	-0.07 ± 2.54	-0.14 ± 2.26	0.87	
Log TVC	-0.84 ± 2.83	-0.18 ± 1.63	0.25	

Caries risk assessment results at baseline and 6 months

Caries risk assessment was performed for each subject at baseline and 6 month visits. Key caries risk assessment for baseline and six month includes three areas of focus:

Disease indicators, Risk factors and Protective factors. Disease indicators used in this evaluation include 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 5, there were no significant differences between groups at baseline for all risk assessment categories.

Evaluation of the data shows trends in the right direction with regards to decreasing caries risk factors with both the control and intervention groups. Looking at baseline percentages we see that within this cohort demographic, the control group shows 46% with current restorations, and 40% for the intervention group. At six months we see a dramatic rise to 72% in both control and intervention groups and all cavitated caries lesions were filled by 6 months.

When we look at risk factors such as heavy plaque, we saw a minimal decrease in both groups from baseline to six months, control group 42 to 40%; and intervention group 57% to 52%. Snacking frequency stayed essentially the same in the control group, but there was a drop from 47% to 38% in the intervention group after six months. The same was noted for deep pits and fissures: baseline for the intervention group was 53% and dropped to 48%, presumably due to restoration and sealant placement. Unstimulated

saliva flow was adequate in all subjects. Only two children were on saliva decreasing medications at the beginning of the study, both appeared the in intervention group.

In the protective factor areas, tooth-brushing frequency showed positive changes in both the control and intervention groups. Reported brushing no times a day went down in the control group from 15% to 12%, and substantially lowered in the intervention group, 17% to 0% at six months. One time a day brushing went down in the control group but only minimally decreased in the intervention group at six months. In both the control and intervention groups we see almost identical increases from baseline to six months in those who brushed two times per day 57% to 72% and 56% to 72% respectively. As expected, in both groups, professional fluoride application rates within last six months increased substantially: controls went from 24 to 65% and the intervention group from 40 to 89% due to tight recall therapy. Overall caries risk categories stayed unchanged, mainly due to the fact that within this cohort nearly all subjects were high caries risk at baseline due to the fact that most all had active caries lesions and required dental restorative care.

The intervention group had a significantly higher probability to have inadequate saliva flow than control group ($P < 0.0001$) but had no significant difference in other risk assessment variables. This may be resulted from that there were more children with medications affecting salivary flow placed in the intervention group. See table 5.

Table 5. Caries Risk Assessment at baseline and 6 month

	Control		**Intervention**	
	Baseline **# subjects (%)** **n=26**	**6 month** **# subjects (%)** **n=25**	**Baseline** **# subjects (%)** **n=30**	**6 month** **# subjects (%)** **n=29**
Restore < 3yr	12 (46.15%)	18 (72.00%)	12 (40%)	21 (72.41%)
Heavy Plaque	11 (42.31%)	10 (40.00%)	17 (56.67%)	15 (51.72%)
Snacking Freq > 3x daily	8 (30.77%)	8 (32.00%)	14 (46.67%)	11 (37.93%)
Deep Pits/fissures	11 (42.31%)	13 (52.00%)	16 (53.33%)	14 (48.28%)
Adequate Unstimulated Saliva	26 (100%)	25 (100%)	30 (100%)	29 (100%)
Saliva Decreasing Medications	0 (0.0%)	0 (0.0%)	2 (6.67%)	1 (3.45%)
TB Freq (%) **0** **1xd** **2xd**	 4 (15.38%) 7 (26.92%) 15 (57.69%)	 3 (12%) 4 (16.00%) 18 (72.00%)	 5 (16.67%) 8 (26.67%) 17 (56.67%)	 0 (0%) 8 (27.59%) / 21 (72.41%)
Pro Fluoride (%) **0** **1**	 12 (48%) 7 (28%) 6 (24%)	 7 (26.92%) 2 (7.69%) 17 (65.38%)	 13 (43.33%) 5 (16.67%) 12 (40%)	 3 (10.34%) 0 (0%) 26 (89.66%)
Adequate Saliva flow	24 (92.31%)	14 (56.00%)	28 (93.33%)	29 (100%)
Over all CRA risk category **High** **Medium** **Low**	 25 1 2	 29 1 1	 22 1 2	 27 1 1

Per CAMBRA protocol, to evaluate, past, present and future caries susceptibility, specific caries risk questions must be evaluated and measured. As stated previously, the focus was placed on specific subjective and objective criteria. The first risk factor evaluated at both baseline and the six month mark is previous restorations placed less than three years. The next risk factor was plaque present, and was categorized as either "yes" or "no" if observable plaque could be seen on teeth during exam. Subjective self-report on snacking frequency greater than three times per day was asked to evaluate if the child regularly engaged in pathologic snacking behavior. Evaluation of pits and fissures along with unstimulated saliva flow are anatomical/physiologic markers which will 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.

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 over all 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, over all caries risk status was evaluated for each subject at baseline and six months by rating all risk factors (disease indicators, risk verses protective factors).

Discussion:

Dental caries is a multifactor infectious disease. Studies have shown that simple caries removal and placement of restorations did not reduce caries risk. The progression of dental caries is determined by the balance between the caries risk factors and preventive factors. 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.[14] The aim of current study is to investigate feasibility and effectiveness 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.

One main preventive regimen in the intervention group is to daily home use of xylitol mints to reduce or modify cariogenic bacteria in high-risk children. The instructed daily xylitol dosage for each child in the intervention group is 6-8 grams per day which reaches the therapeutic dosage of xylitol per previous studies.[63] Our study showed that there were only slight reduction of logMS and logLB in the intervention group with no significant differences to baseline or control group. This result is consistent with previous studies which have shown that short-term xylitol consumption has been shown to decrease 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.[54, 55] 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, flattening out by nine months. [52, 63, 69] This initial decrease followed by a return to baseline is thought to be due to selection of Xylitol resistant strains of MS.[63, 65]

A study by Soderling et al on maternal use of xylitol showed a significant reduction of MS colonization in their children but no change of MS levels in mothers, indicating that xylitol use may prevent caries by modifying cariogenic bacterial virulence or ecology rather than the bacteria loading alone. Therefore, it is impossible to predict the effectiveness of daily xylitol mints use by bacterial loading at six months. Further evaluation of the cariogenic bacterial virulence or caries prevalence at one year will be needed to assess the true effectiveness of daily xylitol mints in 5-9 year old children.

In addition, for xylitol therapy to be effective in reducing MS, and thus caries, the subject must take between 6-8 grams of Xylitol per day. It has been clearly shown that there exists a dependant relationship with regards to dosage and frequency of xylitol ingestion and MS levels. 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.[63] Thus, in our study, it is proposed that for peak effectiveness, xylitol mint dose and frequency would also need to be consistent at 8 grams per day, divided into 3-4 intervals, morning, afternoon and evening. A 3-4 times per day regimen is standard protocol for many medications, such as

short-term antibiotics as well as long-term anti-hypertension, anxiety, and oral anti-hypoglycemics. Such medication compliance is thought to be reasonable and attainable for both short and long term therapy. If there is a daily decrease in number of grams ingested and/or the frequency of ingestion is altered, the caries inhibitory properties of xylitol therapy will be compromised.

Fluoride use plays a significant role in caries prevention by enhancing remineralization and inhibiting of demineralization. However, in 5-9 year old children are still at risk for fluorosis in developing posterior permanent teeth. The current protocol modifies the adult daily home high fluoride content product use to more frequent office use fluoride varnish. This modification decreases the risk of fluorosis by lowering the cumulative systemic ingestion of daily at home high fluoride use as well as helps to avoid the issue of non-compliance that is typical of home use products.

Historically, test subject recall and retention within low income, inner city, non-native language speaking clinical trials has proven challenging for public health researchers.[41] Dental appointment no-show rates at community dental clinics are often as high as 20-40% of scheduled patients.[70] With these subject demographic limitations and challenges in mind, selecting a clinic/research site within an elementary school seems an ideal solution to maximize study subject recall rates and maximum control over dental therapy. Aside from the three children absent during the six month exam week and three transferring to different schools, 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 has increased dramatically from 40% to 90% in the intervention group and 24% to 60% in the control group. We are hoping this would have a significant impact on caries prevention at one year.

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. Second, children miss much less classroom education time due to not having to leave premises or travel. Third, is financial loss as parents did not have to lose income from missing work or for travel expense. And fourth, 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 access and children's dental health within this population. However, it is clear coming from the experience of conducting this clinical trial, having such consistent and reliable access to a population of children has allowed the dental team to ideally manage their oral hygiene and treatment needs. It appears that such a model could be one of the

most effective methods in addressing dental treatment disparities within this demographic. Our result shows that 90% of high risk subjects received fluoride varnish per protocol at baseline and at 6 months.

The oral hygiene and diet habits play important roles in caries balance. In the current study, we included itemized handout to parents and counseling to the children every three month to study whether this could be an effective modality to manage risk factor and promote preventive behavior in high-risk children. The study showed that changes in caries risk status both intra and inter study groups showed a positive trend reduction of risk, and an increase in protective factors even though they were not statistically significant. Having restorations within the last three years is 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 high caries incidence, as seen from the initially high, and then dramatic increase in baseline previous restorations to six month levels: 46-72% and 40-72% 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 significant positive self-reports of increase frequency. Unfortunately, this increase in brushing frequency didn’t correlate with an actual reduction in plaque scores, as there was only a slight decrease in both groups from baseline. The same was

shown for snacking frequency. It would appear that even though all children received standard oral hygiene and diet counseling (significantly more in the intervention group), there appears to be little change in actual behavior. It was hoped that intensive and more frequent instruction and counseling would dramatically improve these behaviors in this model. It is possible that the children are in fact brushing more frequently, but not effectively. Also, we cannot overlook that the subjects may be telling the investigator "what they think they want to hear" to seek approval and not disappoint.

Caries risk data reveals a significant higher probability to have adequate saliva flow in intervention group as compared to controls. This is an unexpected finding within this study. It can be interrupted in two ways: One, children in the control group exhibit a higher incidence of inadequate saliva flow. The other is that regular xylitol mints cause an increase in incidence of adequate saliva flow. It is well known physiologically that chewing gum or sucking on hard candies increases transient saliva rates. Thus one could extrapolate from this data that regular ingestion of xylitol mints may cause an increase in long term salivary flow, however there are no other studies to the authors knowledge that corroborate this explanation. These findings are more likely to be explained by a data collection anomaly.

Only tooth brushing frequency and professional fluoride application showed slight, non-significant increases between control and intervention groups. Plaque scores also were reduced slightly from intervention group compared to controls, but again these changes were not significant. All other caries risk data showed no significant differences.

Limitations:

There are many advantages of having a children's dental clinic on-site in an inner city public elementary school grounds. However, there are also some limitations to this delivery system as well. In particular, communication with parents in this setting when oral hygiene or treatment options which are need to be discussed for maximum effectiveness is often difficult mainly due to the fact that the children were not accompanied by their parents at the dental visit. Second was language, limited phone access, or parental location or accessibility issues. Often the clinic would have no choice but to communicate through written returnable take home information packets (which require a signature). Equally as often the primary language spoken by parents was rarely English, and thus staff translators would be utilized for verbal communication or written information would have to be translated. It wasn't uncommon for many parents to work more than one job and thus became virtually inaccessible via phone or unable to visit the clinic during both business and after hours to discuss treatment options, oral hygiene or answer questions. Thus, communication with parents/caregivers was routinely difficult, time-consuming, labor intensive and sometimes lacking in this study.

Recruitment of study subjects was also complicated in this setting for similar reasons as stated above, and alternative measures were necessary to make contact and inform parents or guardians of the study. As opposed to a traditional dental clinic setting where a parent or guardian would accompany a child to the dental visit, in this school based

model, rarely were the parents or guardians present. For recruitment, instead of personal one on one contact with the parent or guardian, the study had to rely on indirect advertizing and recruitment through administrator-teacher-parent contact, flyers, and take home information. 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 factors at play that may not be encountered at standard community based pediatric dental clinics.

It is well known in the dental community that changing an individual's oral hygiene behavior at home when away from the dental office is extremely challenging. Often the practitioner may feel change is futile with both adult and child patients. Discussion, demonstrations, question and answers, involving the individual along with regular and repeated exposure to such activities are done with the hope of tipping the balance and helping the individual (or parents) make the choice to change destructive behavior(s) to those which are positive. However, with any type of health education geared to change behavior, the burden ultimately rests on the individual, or with children, on the parents. Thus, a limitation in this study, as well as of all dentistry, is that the practitioner has little control of oral hygiene and diet compliance once the patient leaves the office. Within this study, the issue becomes even more challenging because those ultimately responsible, (ie. the parents) are not physically present to receive the message personally, and instead

must receive this information indirectly through the child subject or through written means.

It this study the researchers hoped repeated oral hygiene education both verbal and with written reminders at three months would dramatically affect the child's at home behavior. It appears from the data that such intensive education has caused brushing frequency to change favorably. However, as stated previously, it appears that either the child subject is telling the researcher "what they want to hear" or the quality of the more frequent brushing hasn't improved, when looking at the plaque scores. Because brushing and snacking frequency rely on "self report", and historically these self-reports can come with a large error of unreliability, the results can only be taken with consideration when looking at statistical change within these categories.

Regarding xylitol mint therapy, one of the major limitations to any take-home medication based therapy is patient (parental) compliance. It is well documented in the medical literature [71-73] that compliance rates of at-home self delivered medication regimens on average are low and frequently inconsistent. Missed or incomplete medication ingestion can result in sub-therapeutic doses thus either mitigating or eliminating the medications beneficial therapeutic properties. This is a well-studied and challenging behavioral component of medicine which is not easily controlled by the practitioner. Examples of the negative effects of patients lack of self regulation or ability to follow treatment regimens is readily apparent if one takes a glance at our countries current levels of cardio-vascular disease, type II diabetes, alcoholism, periodontal disease, obesity and

caries rates, all which have a huge behavioral component attached to their cause, and essentially all are preventable and controlled by individual lifestyle choice.

One of the main challenges within this study was attempting to monitor and regulate xylitol mint therapy, whether or not the parents were able to deliver the quantity and timing of mints as prescribed over the course of the study. As stated earlier in this paper, for xylitol to have it's maximum benefits as an anti-caries agent/therapy, a total of eight grams needs to be ingested per day, split into even and regular intervals. Obviously, this type of regimentation can be challenging even for the most organized of individuals. Due to the limitations of parental contact within this study, the researchers had to rely on the quarterly questionnaire for the parents and the child patient self-reports. Because parents were not expected to be onsite routinely, the researchers could not have parents physically bring mint bottles in to appointments to check amount left over as other studies have done to account for medication compliance. Because the researchers were not able to directly count residual mints during the course of the study, actual 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.

Conclusions:

The goal of this study was to address the effectiveness of a modified CAMBRA protocol for 5-9 year-old children who emphasize better diet modification, more frequent

professional fluoride applications, and xylitol product usage based on individual risk status in a 6 month randomized controlled clinical trial in the University of California, San Francisco (UCSF) Tenderloin Elementary School Pediatric Dental Clinic. Our studied showed that after six months of xylitol mint therapy and three-month fluoride varnish placement there was a minimal, but not statistically significant decrease in MS, LB and TVC levels at six months in the test subjects as compared to the controls. These findings are consistent with other xylitol therapy clinical trials. Caries risk assessment variables were found to be a slight decrease in plaque and an increase in tooth brushing behaviors that decreased risk in the intervention group as compared to the controls, but again these differences were not statistically significant.

Although the results of this six-month 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. It should be noted that lowered MS and LB bacterial levels alone don't appear to be the main contributing factor in the caries protective properties of xylitol therapy. Increased dental visit frequency, oral hygiene information and instruction appears to have a positive, albeit not statistically significant effect on tooth brushing frequency and thus overall oral hygiene within this group over the short term. It is also important to point out that the results showed overall xylitol mint at home compliance rates were low and thus a six month regimen of 3-4 times per day may not be realistic nor attainable.

This study only looked at six months worth of data. A one-year continuation of this study is necessary, and is being conducted currently to conclusively 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.

References

1. Rockville, M., *Oral Health in America: A Report of the Surgeon General.* . 2000, U.S. Department of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health.
2. Hyattsville, M.C.f.D.C.a.P.C., unpublished data., *National Health and Nutrition Examination Survey III, 1988–1994*. 1994, National Center for Health Statistics (NCHS). .
3. Vargas, C.M., J.J. Crall, and D.A. Schneider, *Sociodemographic distribution of pediatric dental caries: NHANES III, 1988-1994.* J Am Dent Assoc, 1998. **129**(9): p. 1229-38.
4. Featherstone, J.D., *Dental caries: a dynamic disease process.* Aust Dent J, 2008. **53**(3): p. 286-91.
5. Liljemark, W.F. and C. Bloomquist, *Human oral microbial ecology and dental caries and periodontal diseases.* Crit Rev Oral Biol Med, 1996. **7**(2): p. 180-98.
6. Caufield, P.W., et al., *Natural history of Streptococcus sanguinis in the oral cavity of infants: evidence for a discrete window of infectivity.* Infect Immun, 2000. **68**(7): p. 4018-23.
7. Li, Y. and W. Wang, *Predicting caries in permanent teeth from caries in primary teeth: an eight-year cohort study.* J Dent Res, 2002. **81**(8): p. 561-6.
8. Beltrán-Aguilar ED, B.L., Canto MT, Dye BA, Gooch BF, Griffin SO, Hyman J, Jaramillo F, Kingman A, Nowjack-Raymer R, Selwitz RH, Wu T, *Surveillance for dental caries, dental sealants, tooth retention, edentulism, and enamel fluorosis--United States, 1988-1994 and 1999-2002. MMWR Surveill Summ, Aug 26;54(3):1-43*, in *MMWR Surveill Summ.* 2005, Centers for Disease Control and Prevention (CDC). . p. 1-43.
9. Alaluusua, S., *Salivary counts of mutans streptococci and lactobacilli and past caries experience in caries prediction.* Caries Res, 1993. **27 Suppl 1**: p. 68-71.
10. Leverett, D.H., et al., *Caries risk assessment by a cross-sectional discrimination model.* J Dent Res, 1993. **72**(2): p. 529-37.
11. Featherstone JD, G.S., Hoover CI, LI L, Weintraub JA, and White JA. , *Cariogenic Bacteria Trends in a Randomized Caries Management Clinical Trial.* J. Dent. Res., 2002. **IADR/AADR/CADR 80th General Session (March 6-9, 2002)Abstract 3813**
12. Agriculture, U.S.D.o., *Profiling Food Consumption in America.* 2005.
13. Johansson, I., et al., *Snacking habits and caries in young children.* Caries Res. **44**(5): p. 421-30.
14. Featherstone, J.D., *The caries balance: the basis for caries management by risk assessment.* Oral Health Prev Dent, 2004. **2 Suppl 1**: p. 259-64.
15. Touger-Decker, R. and C. van Loveren, *Sugars and dental caries.* Am J Clin Nutr, 2003. **78**(4): p. 881S-892S.
16. Dentistry., A.A.o.P., *Policy on dietary recommendations for infants, children, and adolescents.* Pediatr Dent 2008. **30(suppl)**: p. 47-8.
17. US Dept of Agriculture, U.D.o.H.a.H.m.S. *Dietary Guidelines for Americans. 6th ed. Washington, DC: US Dept of Agriculture and US Dept of Health and Human*

Services; 2005. 2007 [cited; Available from: http://www.health.gov/dietary guidelines/dga2005/document/
18. Mobley, C., et al., *The contribution of dietary factors to dental caries and disparities in caries.* Acad Pediatr, 2009. **9**(6): p. 410-4.
19. Krebs, N.F. and M.S. Jacobson, *Prevention of pediatric overweight and obesity.* Pediatrics, 2003. **112**(2): p. 424-30.
20. Ritchie, C.S., et al., *Nutrition as a mediator in the relation between oral and systemic disease: associations between specific measures of adult oral health and nutrition outcomes.* Crit Rev Oral Biol Med, 2002. **13**(3): p. 291-300.
21. Romito, L.M., *Introduction to nutrition and oral health.* Dent Clin North Am, 2003. **47**(2): p. 187-207, v.
22. Soderling, E., *Nutrition, diet and oral health in the 21st century.* Int Dent J, 2001. **51**(6 Suppl 1): p. 389-91.
23. Touger-Decker, R. and C.C. Mobley, *Position of the American Dietetic Association: Oral health and nutrition.* J Am Diet Assoc, 2003. **103**(5): p. 615-25.
24. Featherstone, J.D., *The science and practice of caries prevention.* J Am Dent Assoc, 2000. **131**(7): p. 887-99.
25. *For the dental patient: Diet and tooth decay.* J Am Dent Assoc, 2002. **133**(4): p. 527.
26. Jenson, L., et al., *Clinical protocols for caries management by risk assessment.* J Calif Dent Assoc, 2007. **35**(10): p. 714-23.
27. Weinstein, P., R. Harrison, and T. Benton, *Motivating parents to prevent caries in their young children: one-year findings.* J Am Dent Assoc, 2004. **135**(6): p. 731-8.
28. Rozier, R., *Effectiveness of methods used by dental professionals for the primary prevention of dental caries.* Journal of Dental Education, Oct 2001.
29. Moynihan, P.J., *Dietary advice in dental practice.* Br Dent J, 2002. **193**(10): p. 563-8.
30. Ahovuo-Saloranta, A., et al., *Pit and fissure sealants for preventing dental decay in the permanent teeth of children and adolescents.* Cochrane Database Syst Rev, 2008(4): p. CD001830.
31. Llodra, J.C., et al., *Factors influencing the effectiveness of sealants--a meta-analysis.* Community Dent Oral Epidemiol, 1993. **21**(5): p. 261-8.
32. Beltran-Aguilar, E.D., et al., *Surveillance for dental caries, dental sealants, tooth retention, edentulism, and enamel fluorosis--United States, 1988-1994 and 1999-2002.* MMWR Surveill Summ, 2005. **54**(3): p. 1-43.
33. Seppa, L., *Fluoride varnishes in caries prevention.* Med Princ Pract, 2004. **13**(6): p. 307-11.
34. Directors, A.o.S.a.T.D., *Fluoride varnish: and evidence-based approach, .* 2007.
35. Administration, U.S.F.a.D., *Fluoride Varnish.* 2008.
36. Vaikuntam, *Fluoride varnishes: should we be using them?* Pediatr Dent, 2000.
37. VCC Marinho, J.H., S Logan, A Sheiham. , *Fluoride varnishes for preventing dental caries in children and adolescents.* Cochrane Database of Systematic Reviews, 2008.

38. Azarpazhooh, A., *Fluoride varnish in the prevention of dental caries in children and adolescents: a systematic review.* Journal of American Dental Association, 2008.
39. Borutta A, R.G., Hufnagl S, Möbius S. , *Caries prevention with fluoride varnishes among preschool children.* Gesundheitswesen, 2006.
40. Hardman MC, D.G., Duxbury JT, Davies RM, *Fluoride varnish as a public health measure to reduce caries.* Evid Based Dent, 2008.
41. Weintraub, J.A., *Fluoride varnish for caries prevention: comparisons with other preventive agents and recommendations for a community-based protocol.* Spec Care Dentist, 2003. **23**(5): p. 180-6.
42. Weintraub, J.A., et al., *Fluoride varnish efficacy in preventing early childhood caries.* J Dent Res, 2006. **85**(2): p. 172-6.
43. AAPD, *Guidelines for fluoride Therapy.* Americian Acadamy of Pediatric Dentistry - guidelines, 2008.
44. Bawden, J.W., *Fluoride varnish: a useful new tool for public health dentistry.* J Public Health Dent, 1998. **58**(4): p. 266-9.
45. Hardman MC, D.G., Duxbury JT, Davies RM, *Fluoride varnish as a public health measure to reduce caries.* . Evid Based Dent, , 2008.
46. Jenkins, S., M. Addy, and W. Wade, *The mechanism of action of chlorhexidine. A study of plaque growth on enamel inserts in vivo.* J Clin Periodontol, 1988. **15**(7): p. 415-24.
47. Hase, J.C., et al., *6-month use of 0.2% delmopinol hydrochloride in comparison with 0.2% chlorhexidine digluconate and placebo (II). Effect on plaque and salivary microflora.* J Clin Periodontol, 1998. **25**(11 Pt 1): p. 841-9.
48. Featherstone JD, G.S., Hoover CI, Rapozo-Hilo ML, Weitraub JA, White JM, and Wilson RS. , *Chlorhexidine and Fluoride Therapy Reduces Caries Risk* J. Dent Res, 2005. **IADR/AADR/CADR 83rd General Session (March 9-12, 2005) Abstract 0023**.
49. Matthijs, S. and P.A. Adriaens, *Chlorhexidine varnishes: a review.* J Clin Periodontol, 2002. **29**(1): p. 1-8.
50. Autio-Gold, J., *The role of chlorhexidine in caries prevention.* Oper Dent, 2008. **33**(6): p. 710-6.
51. Hayes, C., *The effects of noncariogenic sweeteners on the prevention of dental caries: A review of the evidence.* J Dent Educ, 2001. **65**: p. 1006-1109.
52. Ly, K.A., et al., *Xylitol gummy bear snacks: a school-based randomized clinical trial.* BMC Oral Health, 2008. **8**: p. 20.
53. Milgrom, P., et al., *Xylitol pediatric topical oral syrup to prevent dental caries: a double-blind randomized clinical trial of efficacy.* Arch Pediatr Adolesc Med, 2009. **163**(7): p. 601-7.
54. Hayes, C., *The effect of non-cariogenic sweeteners on the prevention of dental caries: a review of the evidence.* J Dent Educ, 2001. **65**(10): p. 1106-9.
55. Trahan, L., et al., *Effect of xylitol consumption on the plaque-saliva distribution of mutans streptococci and the occurrence and long-term survival of xylitol-resistant strains.* J Dent Res, 1992. **71**(11): p. 1785-91.

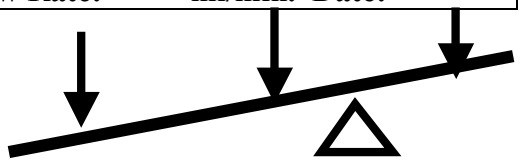
56. Scheinin, A., K.K. Makinen, and K. Ylitalo, *Turku sugar studies. V. Final report on the effect of sucrose, fructose and xylitol diets on the caries incidence in man.* Acta Odontol Scand, 1976. **34**(4): p. 179-216.
57. Soderling, E.M., *Xylitol, mutans streptococci, and dental plaque.* Adv Dent Res, 2009. **21**(1): p. 74-8.
58. Rao, R.S., et al., *Xylitol production from corn fiber and sugarcane bagasse hydrolysates by Candida tropicalis.* Bioresour Technol, 2006. **97**(15): p. 1974-8.
59. (FASEB), F.o.A.S.f.E.B., *Health aspects of sugar alcohols and lactose.* Life Sciences Research Office, Center for Food Safety and Applied Nutrition, Food and Drug Administration, 1986. **FDA 223-83-2020**
60. Forster, H., R. Quadbeck, and U. Gottstein, *Metabolic tolerance to high doses of oral xylitol in human volunteers not previously adapted to xylitol.* Int J VItam Nutr Res, 1982. **22**(suppl): p. 67-88.
61. Tanzer, J.M., *Xylitol chewing gum and dental caries.* Int Dent J, 1995. **45**(1 Suppl 1): p. 65-76.
62. Forster, H., R. Quadbeck, and U. Gottstein, *Metabolic tolerance to high doses of oral xylitol in human volunteers not previously adapted to xylitol.* Int J Vitam Nutr Res Suppl, 1982. **22**: p. 67-88.
63. Milgrom, P., et al., *Mutans streptococci dose response to xylitol chewing gum.* J Dent Res, 2006. **85**(2): p. 177-81.
64. Ly, K.A., et al., *Linear response of mutans streptococci to increasing frequency of xylitol chewing gum use: a randomized controlled trial [ISRCTN43479664].* BMC Oral Health, 2006. **6**: p. 6.
65. Krupansky C, F.J., Den Besten P, Hoover C, Zhan L *Effectiveness of Xylitol on Maternal Bacterial Transmission to Infants.* , in *AAPD annual General Session (GSRA annual Award)*. 2009: Honolulu, Hawii.
66. Domejean-Orliaguet, S., S.A. Gansky, and J.D. Featherstone, *Caries risk assessment in an educational environment.* J Dent Educ, 2006. **70**(12): p. 1346-54.
67. Featherstone, J.D., et al., *Caries risk assessment in practice for age 6 through adult.* J Calif Dent Assoc, 2007. **35**(10): p. 703-7, 710-3.
68. Domejean, S., et al., *Horizontal transmission of mutans streptococci in children.* J Dent Res, 2010. **89**(1): p. 51-5.
69. Thaweboon, S., B. Thaweboon, and S. Soo-Ampon, *The effect of xylitol chewing gum on mutans streptococci in saliva and dental plaque.* Southeast Asian J Trop Med Public Health, 2004. **35**(4): p. 1024-7.
70. Diringer, J., *Expanding Access to Dental Care Through California's Community Health Centers.* 2007.
71. Hudson, T.J., et al., *Guideline implementation and patient-tailoring strategies to improve medication adherence for schizophrenia.* J Clin Psychiatry, 2008. **69**(1): p. 74-80.
72. Laufs, U., et al., *[Strategies to improve medication adherence].* Dtsch Med Wochenschr. **136**(31-32): p. 1616-21.
73. Warren, S.R., et al., *Medication adherence assessment in a clinical trial with centralized follow-up and direct-to-patient drug shipments.* Clin Trials.

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.

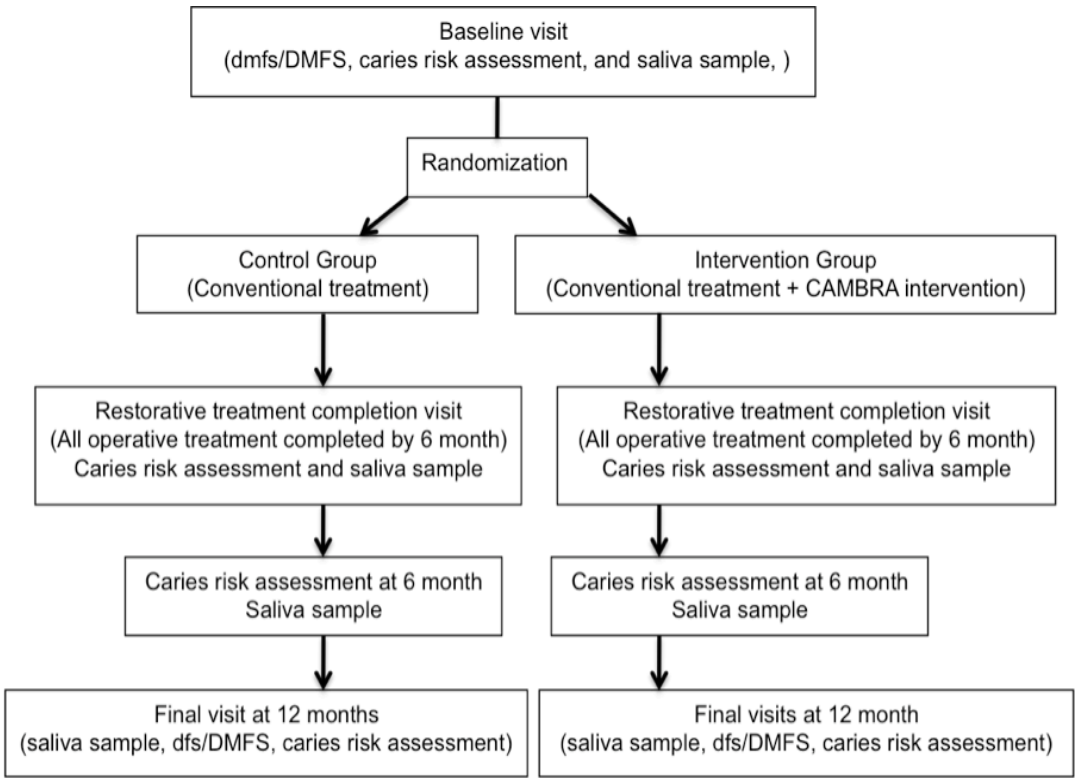
a. If your child is assigned to the control group
    i. They will continue to receive regular dental care, such as dental restorations and 6 month checkups, cleanings and fluoride therapy, no different then your child's current care.
    ii. At each 6 month checkup and cleaning visit your child will 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.

Study Chart



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

Publishing Agreement

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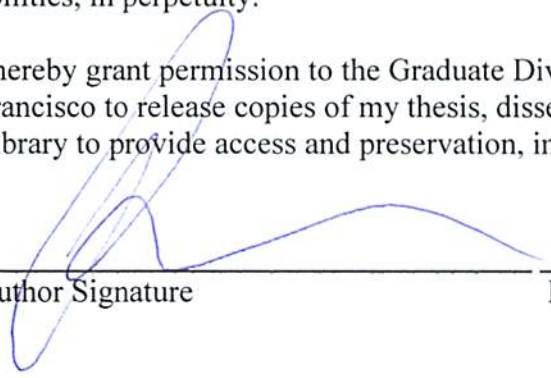

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