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A Pilot Study to Evaluate the Effect of Livionex on Reducing Plaque Accumulation and Oral Health in Children

by
Lesley Latham

THESIS
Submitted in partial satisfaction of the requirements for degree of
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in

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in the

GRADUATE DIVISION
of the
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Approved:

DocuSigned by:
Thuan Le ______ Thuan Le
A3AFA95F85E54DE...
Chair

DocuSigned by:
Pam Den Besten ______ Pam Den Besten
D38B9392AD432...

DocuSigned by:
BRENT LIN ______ BRENT LIN
38FA9C8D5943431...

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Committee Members

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M.S. Thesis Committee Members

Dr. Thuan Le

Dr. Pamela Den Besten

Dr. Brent Lin

A Pilot Study to Evaluate the Effect of Livionex on Reducing Plaque Accumulation and Oral Health in Children

Lesley Latham

Abstract

Purpose: To determine whether the effectiveness of the test dental gel: fluoride-free Livionex Dental Gel® was equivalent to that of a control dental gel, which contained 1100 ppm fluoride, in reducing oral plaque and preventing new dental decay in a high caries risk pediatric population.

Methods: This study was a prospective, double-blinded, randomized, controlled trial pilot and non-inferiority trial exam, consisting of bleeding index, clinical photographs, plaque index, caries prevalence, dental X-rays, oral hygiene instruction, and saliva bacterial sample collect for analysis to be compared across timepoints.

Results: 63 subjects (33 in Livionex and 30 in control) participated. Caries prevalence and incidence remained comparable between the control and intervention groups. There were no significant differences in bleeding, and plaque levels.

Conclusions: Livionex is not inferior to the gold-standard toothpaste in caries and plaque prevention. The dental gel is a good alternative for populations affected by fluoride and other additives.

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Introduction

Toothpastes are used to clean the tooth surfaces with the use of a toothbrush, to improve oral health. Most toothpastes include abrasives and detergents to mechanically remove dental plaque, flavoring agents, and other additives focused toward addressing various oral diseases including plaque, calculus, caries, gingival inflammation, and periodontitis. Fluoride is frequently added to toothpaste due to its cariostatic effects (Kanduti et al. 2016) to promote remineralization by enhancing the precipitation of calcium and phosphate from saliva to deposit minerals into demineralized tooth tissues.

When chronically swallowed, fluoride contained in toothpastes increases the incidence of enamel fluorosis. While enamel fluorosis is largely considered by the dental community as only of esthetic concern (McGrady et al. 2012), recent population based studies that have shown effects of ingested fluoride on neurodevelopment (Bashash et al. 2018; Green et al. 2019; Malin and Till 2015; Riddell et al. 2019; Thomas et al. 2016), have led to considerations of alternatives that are as effective as fluoride containing toothpastes for dental caries prevention (Cheng et al. 2007).

Livionex tooth gel is a fluoride-free oral care product that uses the active ingredients of EDTA and methylsulfonylmethane (MSM), to disrupt calcium bonds which maintain oral microbiome biofilms in the mouth. Use of Livionex has been shown to have positive effects on biofilm related oral health by reducing gingival inflammation (Shoeb et al. 2018; Wang et al. 2015; Zhang et al. 2009) and periodontal pocket depth (Lin et al. 2019).

In addition to reducing calcium bonding in the biofilm, a micro-chelator, such as EDTA in Livionex, may also possibly disrupt the calcite mineral layer that is produced by bacteria. This calcite layer has been shown to strengthen the biofilm structure, and to protect bacteria from treatments such as antibiotics (Keren-Paz et al. 2020; Oppenheimer-Shaanan et al. 2016).

Dental caries is caused by the demineralization of tooth enamel by acid producing bacteria within the plaque biofilm covering the tooth surfaces. Livionex tooth gel is therefore a promising alternative to alter the plaque biofilm as a means to reduce plaque bacteria and protect teeth from acid demineralization associated with these bacteria. To assess this possibility, we conducted a non-inferiority clinical trial, to determine whether or not Livionex tooth gel was inferior to regular fluoride containing toothpastes.

Background

Dental caries is defined as "a biofilm-mediated, diet modulated, multifactorial, non-dynamic disease, resulting in net mineral loss of dental hard tissues (Machiulskiene et al. 2020). As a consequence of this process, a caries lesion develops. The tooth biofilm, or dental plaque, contains a bacteria ecosystem, the balance of which shifts to acid producing bacteria in the presence of increased sugar or fermentable carbohydrates consumption. The most virulent of these acid producing species, *Streptococcus mutans (S. mutans)*, has been found to be the initiator of most dental caries. *S. mutans* requires a solid, non-shedding surface for colonization, and attaches to surfaces with an adhesive glucan, that is synthesized from sucrose by the action of glucosyltransferases (Kawabata and Hamada 1999).

Demineralization of mineralized tooth structures by acid produced in the bacterial biofilm is modulated by saliva. Saliva contains bicarbonate to buffer the acid produced by cariogenic and aciduric bacteria (Loesche 1986), and is supersaturated with calcium and phosphate ions, which precipitates to form hydroxyapatite and remineralizes the tooth surfaces. Therefore, a balance exists between the amount of acid produced by aciduric bacteria, pH buffering by saliva, and remineralization (Featherstone 2004).

Regular removal of biofilm on the tooth and the incorporation of fluoride in toothpaste has been the mainstay of dental caries prevention. Toothpastes generally use abrasives and detergents to loosen the biofilm, and fluoride to enhance the rate of precipitation of calcium and phosphate from saliva to demineralized surfaces. However, while abrasives in toothpaste are effective in partially removing the biofilm, the majority of adults using a manual toothbrush have difficulties in achieving adequate plaque control (Van der Weijden et al. 1993). For children this task becomes even more difficult to accomplish as manual dexterity is not fully developed in most children before the age of six.

Fluoride is added to toothpastes to enhance mineral precipitation from the saliva to repair early demineralized enamel lesions. However, because toddlers and young children mostly swallow rather than spit out toothpaste, fluoride chronically ingested in toothpastes is also associated with increased dental fluorosis. Fluorosis in the permanent central incisors and first permanent molars is associated with fluoride ingestion in the first 2 years of life (Hong et al. 2006); and in later erupting teeth, it is associated with fluoride ingestion through until about 8 years of age (Bhagavatula et al. 2016).

While dental fluorosis is considered by many to be of only of esthetic concern, fluorosis is also a biomarker for the extent to which fluoride has altered cell function during enamel formation. This suggests the possibility that fluoride could also affect cellular mechanisms in other tissues and organs developing during the same time of exposure. In support of this, recent studies have shown that fluoride exposure in utero and in the first year of life can affect the developing brain

(Bashash et al. 2018; Bashash et al. 2017; Choi et al. 2012; Ding et al. 2011; Green et al. 2019; Malin and Till 2015; Riddell et al. 2019; Tang et al. 2008).

These findings direct us to reassess the risk benefit ratio of ingested fluoride for vulnerable populations, such as the unborn or young child. One strategy for reducing fluoride ingestion in young children has been the recommendation to limit the amount of fluoridated toothpaste used by young children. The Center for Disease Control (CDC), along with the American Academy of Pediatrics (AAP), American Academy of Pediatric Dentistry (AAPD), and American Dental Association (ADA) recommend fluoride toothpaste for all children and limit the amount of toothpaste used by children aged <3 years to a “smear” layer or the size of a grain of rice (Thornton-Evans et al. 2019). Reducing the amount of toothpaste used to brush a child’s teeth will likely reduce the incidence of fluorosis that results from swallowing the toothpaste. However, it also reduces the concentration of fluoride in the saliva, which could reduce the effectiveness of this topical fluoride exposure in caries prevention (DenBesten and Ko 1996).

Some alternatives to fluoride-containing toothpastes include the incorporation of microcrystalline hydroxyapatite to enhance remineralization. A non-inferiority study in orthodontic patients showed no significant differences in the effectiveness of a microcrystalline hydroxyapatite containing fluoride-free toothpaste and a control toothpaste containing 1400 ppm fluoride (Schlagenhauf et al. 2019).

Another approach for caries prevention is to focus on strategies that may directly affect the plaque biofilm. Livionex dental gel alters the plaque biofilm by using MSM (methylsulfonylmethane) to facilitate the transport of the calcium chelator, EDTA (ethylene diamine tetracetic acid), into the biofilm. The assumed mechanism is that once inside the plaque biofilm, EDTA chelates and disrupts calcium bonds that are responsible for stabilizing the bacteria biofilm. Studies show significant reductions in plaque accumulation (Anbarani et al. 2018), gingival inflammation, and periodontal pocket depth (Lin et al. 2019) with the use of Livionex as compared to fluoride-containing control toothpastes.

The results of these studies are consistent with the known roles of calcium in biofilm formation. The presence of calcium and magnesium is thought to affect the initial bacterial attachment to surfaces, by assisting in conditioning biofilm formation by bridging between molecules, to modify cell surface adhesins, and reducing the apparent surface charge and surface potential (Wang et al. 2019). In studies of titanium implants, calcium was found to serve as a bridging agent in the adhesion process of *S. mutans*, while removing calcium from the titanium surface by EGTA caused a significant decrease in the adhesion of these bacteria. A similar effect was not observed with *P. gingivalis*, suggesting that calcium specifically enhances adhesion of cariogenic *S. mutans* to surfaces (Badihi Hauslich et al. 2013).

To address a concern that introducing EDTA as calcium chelator into the plaque biofilm may demineralize enamel, a double-blinded, randomized study was done to compare the enamel microhardness and surface morphology of demineralized enamel disks worn with an intraoral device by studied subjects using either Livionex or a regular control toothpaste. After one-week intraoral wear, the enamel chips from both groups fully recovered from demineralization, with no significant difference in microhardness or surface morphology between the two groups ($p > 0.05$) (Anbarani et al. 2017).

Together, these findings support the possibility that fluoride free Livionex dental gel may provide an alternative to fluoride-containing toothpastes for vulnerable populations who swallow rather than spit out toothpaste after tooth brushing. Therefore, the purpose of this study is to determine whether Livionex results in better plaque control and associates with reduced incidence of dental caries for young children (9 months to age of 12 years).

Significance

The use of fluoride containing toothpastes is accepted as a standard of care for caries prevention in children. However, fluoride ingestion by young children is a major concern both because of its association with increased dental fluorosis, and the association between ingested fluoride neurotoxic effects in unborn and young children. An alternative effective strategy to reduce cariogenic oral bacteria, without the use of fluoride, is therefore an important goal to explore.

Hypothesis

The study hypothesis was that brushing with Livionex dental gel would result in greater plaque reduction, and caries inhibition equal to that of children's toothpaste containing 1100 ppm fluoride, in a high caries risk pediatric population.

Materials and Methods

Study Design

This study was a prospective, double-blinded, randomized controlled trial pilot non-inferiority trial to determine whether the effectiveness of the test dental gel: Livionex Dental Gel® (Livionex, Los Gatos, CA 95030) , was equivalent to that of a control dental gel: (Crest for Kids)®, P&G, Cincinnati, OH 45202), in reducing oral plaque and preventing new dental decay in a high caries risk pediatric population.

Ingredients in Livionex are water, sulfonylbismethane, edathamil, stevia, iota carrageenan gum, konjac gum and lecithin.

Ingredients in the control toothpaste are Stannous Fluoride, Glycerin, Hydrated Silica, Sodium Hexametaphosphate, Propylene Glycol, PEG-6, Water, Zinc Lactate, Trisodium Phosphate, Flavor, Sodium Lauryl Sulfate, Sodium Gluconate, Carrageenan, Sodium Saccharin, Xanthan Gum, Blue 1.

Study Procedures

After the approval of the study by the UCSF Human Research Committee (IRB Study # 15-1829), subjects were recruited from the UCSF Pediatric Dentistry Clinic. Inclusion criteria were healthy children aged 9 months to 12 years, accompanied by parents and children able to complete the study procedures, and willing to participate. Exclusion criteria were language barriers and known allergies to edathamil (trade name for the combination of EDTA and MSM) or multiple hygiene and cosmetic products. After obtaining informed consent from parents and/or patient's assent from minors, subjects were randomized in a 1:1 ratio to the active (Livionex) group and control (Crest for Kids) groups. All toothpastes were packaged by Livionex with identical appearance but different lot numbers. Each child was given an electronic toothbrush as an incentive and was given a $20 gift certificate at each study visit.

Only the study coordinator knew the code key assigned to the dentifrices. All other researchers, assistants, and subjects were blinded. Dental exams were conducted at 5 time points: day 0, and after 3, 6, 9 or 12 months. This study was initially scheduled to end after 9 months. However, for at least half of the study subjects, the 9-month time point coincided with the closure of the pediatric dental clinics due to the COVID 19 pandemic. Therefore, for the remaining subjects, the final exam took place after 12 months.

The exam consisted of bleeding index, clinical photographs, plaque index, caries assessment with a dental probe, and dental X-rays (completed at 6-month intervals according to pediatric dentistry standards of care (http://www.mychildrensteeth.org/assets/2/7/E_Radiographs.pdf). Oral hygiene instructions were given as well as a demonstration of brushing techniques. Surveys of the patient's experience with the dentifrices was conducted at the end of the study (see Table 1: Study Schedule).

Demographic Data

Age, sex, race, ethnicity and socioeconomic status, were retrieved from patient's dental records.

Bleeding Index

Bleeding was assessed as either 0=absent, or 1= present, after the children's teeth were brushed with a toothbrush.

Plaque index

Photos of the 6 maxillary and mandibular incisors (canine to canine) were taken following the use of a plaque disclosing solution at each study visit. The photos were assessed by a single examiner and given a plaque index score**.** This plaque score was evaluated using a simplified Turesky modification of the Quigley-Hein Plaque Index (Turesky et al. 1970). Scores ranged from 0-3; 0=no plaque present, 1=plaque covers <⅓ of gingival half of tooth, 2= plaque covers ⅓ to ⅔ of tooth, 3=plaque covers more than ⅔ of tooth. The total plaque score for anterior teeth, as assessed by the photograph, was divided by the number of teeth present.

New dental decay

Dental caries and restorations were assessed at each visit through the use of manual probing of tooth surfaces and dental X-rays. All caries assessments were done by a single blinded examiner.

The number of carious teeth and carious tooth surfaces were assessed by a single separate examiner.

Follow-up survey and questionnaire

At the end of the study period, a questionnaire was given to the child's guardian to assess the child's reaction to the dental gel or toothpaste. Questions included whether they like the taste, and how often the toothpaste was used (see Fig 1: Final Toothpaste Survey).

Potential risks and study stopping rules

All possible study-related adverse reactions were captured on the study database. If at any time point there was a significant increase in dental caries in children using Livionex as compared to the control toothpaste, the study would be stopped. If there was an indication that the gingival health and plaque control in subjects using Livionex was worse than the control group, the study would also be stopped.

Statistical Analysis

The goal of the study was to recruit a total of 70 young children, with 35 in each group. This was based on the assumption that with 80% power, 35% of the children in the control toothpaste group will achieve dental plaque reduction compared to 70% of the Livonex group. Bleeding, plaque index and plaque progression, and new caries were compared at 3-, 6-, and 9-12 month intervals for safety analysis. Comparisons of plaque, bleeding, and new decay in active as compared to control subjects were done using ANOVA or a Student's t test.

Results

Our initial enrollment contained 78 subjects: 39 Livionex (active) and 39 control group. A total of 15 Livionex and 9 control study subjects were lost to follow-up or withdrew before the final 9- or 12-month visits. The final number of subjects completing the study were 24 in Livionex and 30 in the control group. The difference in the rate of attrition of the Livionex as compared to control group was associated with reports that many of the children using Livionex did not like the (lack of) taste, and the gel-like consistency of Livionex tooth gel, as compared to their regular toothpaste (data not shown).

Subject characteristics

All study subjects enrolled in this study were patients of record at the UCSF pediatric dental clinic. The study subjects were primarily low socioeconomic status (SES), as indicated by their enrollment in the California Medi-Cal program. Of the subjects enrolled, 11 Livionex, and 7 control were lost from the study by 3 months.

The final number of study patients and the timing of their visits were impacted by the Shelter in Place regulations that were put into place for the San Francisco Bay Area, in response to the COVID-19 pandemic (see Table 2). A final number of 21 Livionex and 31 controls completed the final exam.

No significant differences in demographic were found between the intervention and control groups. 60% of the intervention and 45% of the control groups were female. Although 27% of Livionex recipients were African-American, no African-American patients were selected to use the control. The median age of participants was 6 years with the youngest patient at 2.2 years and the oldest at 11.5 years of age. Study subjects at baseline had 1.46 $\pm$ SD 2.89 carious tooth surfaces in the Livionex test group, and 3.00 $\pm$ SD 4.16 in the control group, with no statistically significant difference between groups.

Oral health as measured by bleeding, plaque and new decay showed no significant differences between groups.

There were no significant differences in the bleeding index (see Figure 3) or plaque index (see Figure 4) at 3, 6 or 12 months. However, we did find a significant increase in both plaque and bleeding in the Livionex group at 9 months as compared to the control toothpaste.

There were no significant differences in the amount new decay as compared to baseline in the Livionex as compared to control group (see Figure 3 and Tables 5). A further analysis was conducted to evaluate the equivalence or noninferiority of Livionex dental gel to Crest Kids for reducing dental caries. The simplest and most widely used approach to test equivalence is the two one-sided test (TOST) procedure. Using TOST, equivalence is established at the α significance level if a $(1–2\alpha) \times 100\%$ confidence interval for the difference in efficacies (new therapy – current therapy) is contained within the interval $(-\delta, \delta)$ (Fig. 2). The reason the confidence interval is $(1–2\alpha) \times 100\%$ and not the usual $(1- \alpha) \times 100\%$ is because this method is tantamount to performing two one-sided tests. Thus, using a 90% confidence interval yields a 0.05 significance level for testing equivalence (Walker and Nowacki 2011).

In noninferiority studies, the objective is to demonstrate that a therapy is not inferior (i.e., equivalent or possibly superior) than another. In terms of the equivalence margin, the research hypothesis is that the efficacy of the new therapy is no more than δ units lower than that of the current therapy (when higher is better). Noninferiority is established, at the α significance level, if the lower limit of a $(1–2\alpha) \times 100\%$ confidence interval for the difference (new therapy – current therapy) is above $-\delta$. When efficacy is measured by failure rates, where lower is better, noninferiority is established if the upper limit of a $(1–2\alpha) \times 100\%$ confidence interval is below δ. (Walker and Nowacki 2011) (see Figure 2).

In 9-12 months the confidence interval of the difference in the number of new caries is $-1.00 < -0.26 < 0.47$. Since this 90% confidence interval is entirely below the chosen δ for clinical significance (+2.00) and within the range of the chosen $-\delta$ (-2.00) and δ (2.00), the Livionex (without fluoride) is as good as (non-inferior and equivalent to) Crest for Kids (1,100 ppm fluoride) at 12 months (see Fig 4).

For the ratio of tooth surfaces with caries to total number tooth surfaces, the difference is -1.60% < -0.44% < 0.71%. Since this 90% confidence interval is entirely below the chosen δ for clinical significance (+2.38%) and within the rage of the chosen -δ (-2.38%) and δ (2.38%), the Livionex (without fluoride) is as good as (non-inferior and equivalent to) Crest for Kids (1100 ppm Fluoride) at 12 months.

Using the stated criteria of incidence of new caries and ratio of the tooth surface with new caries to total number tooth surfaces, the Livionex tooth gel (without fluoride) is at least as good as the control Crest for Kids (with 1100 ppm fluoride) and did not place the subjects at an increased risk of developing new caries.

Based on this, the establishment of equivalence is shown in the blue bordered box using these criteria, both equivalence and non-inferiority were established between Livionex and Control using a 90% confidence interval.

Patient Experience and Compliance and effect on outcome

Overall, significantly more children in the Livionex test group reported not liking the toothpaste ($p < 0.001$). Participants particularly found the non-foaming aspect took some time to get used to.

Incidence of Oral and Systemic Adverse Effects

There were no adverse oral or systemic effects reported for any subject.

Discussion

Our finding of either no significant differences, or increased plaque and bleeding in the 9 month exam group, was surprising given previous evidence showing that use of Livionex significantly decreased plaque and gingivitis in adults (Lin et al. 2019). It is possible that this finding reflects brushing as the children in the Livionex group did not like the tooth gel as well as controls. Therefore, reduced brushing and relative use of Livionex as compared to controls may have reduced the effectiveness of Livionex to reduce plaque accumulation.

However, despite the fact that Livionex did not result in increased plaque removal, there were no significant differences in new caries were found when comparing Livionex to the control toothpaste within a 9- or 12-month time period. The children included in this study were categorized as high caries risk due to the number of decayed teeth at their baseline exam (1.46 $\pm$ SD 2.89 carious tooth surfaces in the Livionex test group, and 3.00 $\pm$ SD 4.16 for the control group). At the end of treatment, children in the Livionex group averaged 0.93 $\pm$ 1.88 newly decayed teeth, while the control group averaged 1.19 $\pm$ 2.32 decayed teeth.
TOST analyses showed Livionex to be equivalent and noninferior to the control fluoride containing toothpaste in the prevention of new decay in this high-risk group of children. These findings suggest that though Livionex tooth gel does not contain fluoride, the overall effectiveness in the prevention of new decay was equivalent to a traditional fluoride containing toothpas

Fluoride containing toothpastes remove plaque bacteria through the use of abrasives and promote mineral formation through the use of fluorides. Livionex dental gel does not contain either abrasives or fluoride, suggesting that its caries prevention mechanisms may go beyond simply removing more plaque, but instead Livionex may mediate changes in the composition of the microbial, and the relative number of cariogenic bacteria..

S. mutans produces acid known to contribute to the formation of dental caries. We speculate that Livionex could function by altering the microbial composition or the oral microbiome. If calcium within the dental plaque is reduced, this could inhibit the adherence of *S. mutans* to the tooth surface (Esberg et al. 2017) or destabilizing of layer of mineralized calcite within the biofilm (Wang et al. 2019). Both of these processes could then release calcium ions into the plaque fluid to be available for remineralization of the enamel surface. Additional studies are ongoing to further test this possibility.

In conclusion, from this pilot study we found that Livionex was equivalent and non-inferior to the control fluoridated toothpaste with 1100 ppm fluoride in inhibiting formation of new dental caries. Livionex does not contain either abrasives, which may cause abrasion and remove sound tooth structure, or fluoride, which if ingested may have systemic effect on the developing tooth organs, and other tissues and organs in the body. Instead, Livionex containing EDTA is directed into the tooth surface biofilm through its association with MSM. Further studies to elucidate the mechanism by which Livionex may control caries formation can lead to new alternative dentifrice for caries prevention in vulnerable populations.

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Figures

On the scale 1-3 describe your experience with brushing your child's teeth	**Scale**
Toothpaste taste	
Do not like it all that much	1
It is OK.	2
I like this toothpaste, it is really easy to use.	3
Comfort with teething	
Very fussy/crying a lot when teething	1
Somewhat fussy/crying while teething	2
No problems with teething	3
How many times a day did you usually brush your child's teeth	
Less than once a day	1
Once a day	2
Twice or more a day	3
On a scale 1-3 describe your experience with teeth brushing after last dental exam	
How often did you use other oral health care products along with the toothpaste (ie oral gel for teething or another toothpaste)	
Never	1
Sometimes	2
Often	3

Figure 1. Final Toothpaste Survey

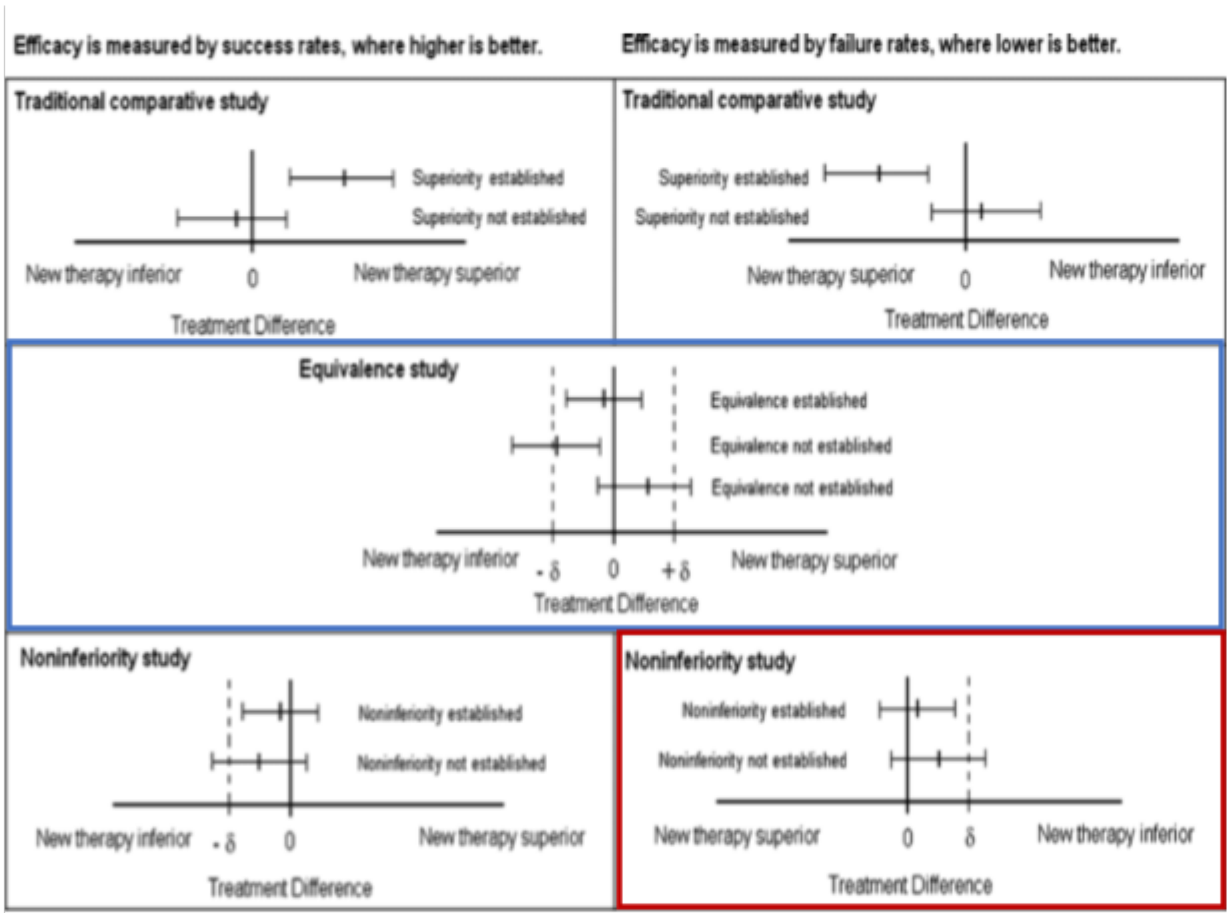

Figure 2. Examples showing TOST in Equivalence (Blue Bordered Box) and Noninferiority (Red Bordered Box) Testing.

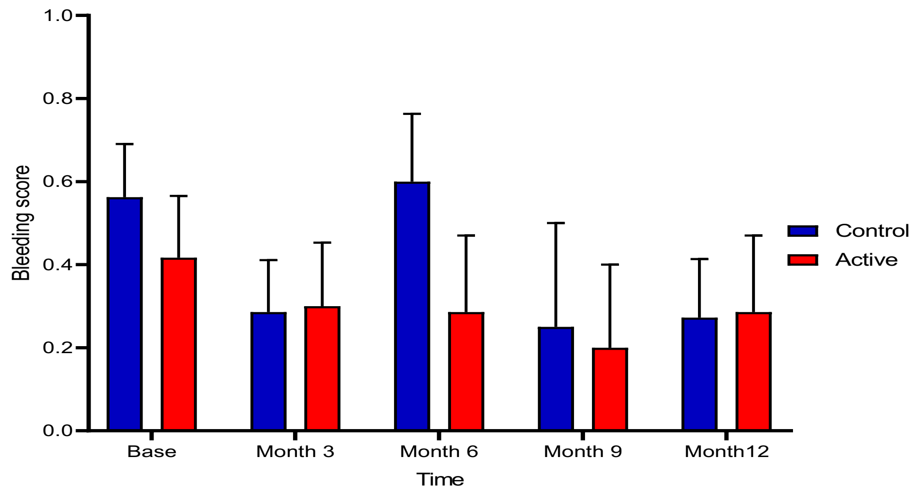

Figure 3: Bleeding Index Change. ANOVA Two-sample t-test assuming equal variance showed no significant differences between groups.

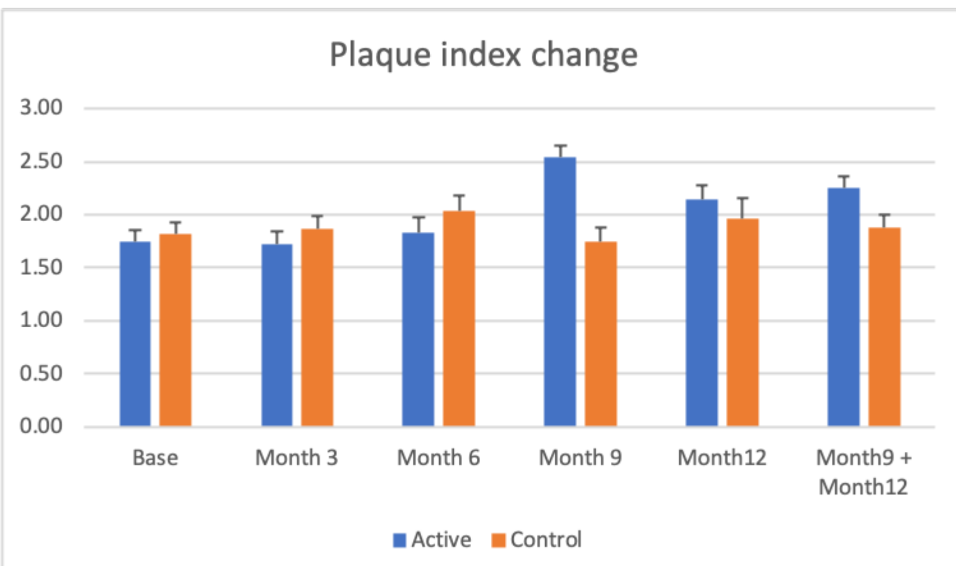

Figure 4. Changes in Plaque levels from baseline every 3 months for one year for the control and intervention groups. *Two Sample t-test assuming equal variance: nine-month recall time yielded significantly (p>0.0005), but not at other time points.

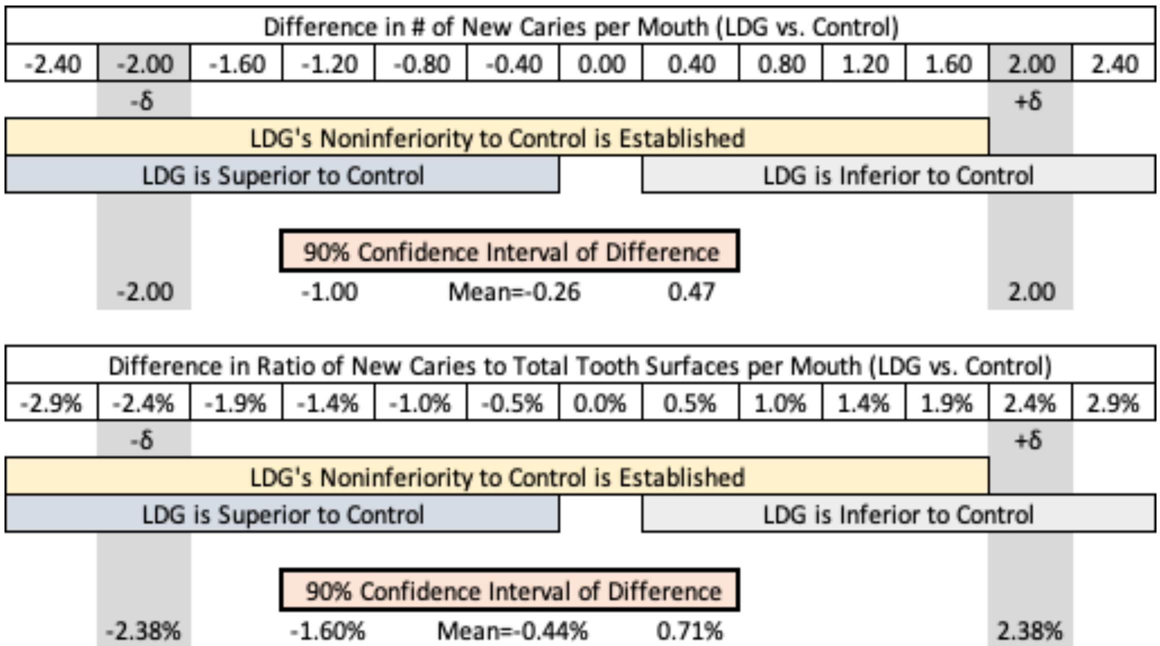

Figure 5. Two One-Sided Test (TOST) at 12 months showed LIvionex dental gel to be equivalent and noninferior to the control toothpaste (Crest for Kids)

Tables

Table 1: Study schedule

	Months			
Procedures	Baseline (day 0)	3	6	9-12
Consent/assent	x			
Randomization	x			
Demonstration of proper teeth brushing	x	x	x	x
Dental and Medical history and updates collection	x	x	x	x
Dental plaque staining and photograph	x	x	x	x
Dental caries assessment	x		x	x
Dental plaque and saliva specimen collection	x	x	x	x
Dentifrice experience and teeth brushing questionnaire				x

Table 2: Number of subjects at each return visit

	Livionex Number	Control Number
Baseline	30	33
3 months	21	28
6 months	17	21
9-11 months	9	13
12-15 months	12	18
Total completing the study at 6, 9 or 12 months*	21	31

Table 3: Subject Demographics

	Livionex Number	Control Number
Subject number	30	33
Gender (female)	18 (60%)	15 (45%)
Ethnicity Not Hispanic	10 (60%)	14 (42%)
White	5 (17%)	9 (27%)
African American	8 (27%)	0
Asian	13 (43%)	7 (21%)
American Indian/Alaska Native	0	7 (21%)
Native Hawaiian	1 (3%)	1 (3%)
Other	13 (43%)	19 (58%)
Declined to answer	0	1 (3%)
Age (years) (median, range)	5.97, 2.2-11.5	6.04, 1.1-10.2
Low SES (Medi-Cal)	27 (90%)	29 (88%)
Carious teeth at baseline (mean, SD)	1.5, 2.9	3, 4.2

Table 4: Effect of Toothpaste use on of new caries. Livionex dental gel (without fluoride) was equivalent/noninferior to the control toothpaste (Crest for Kids with 1100 ppm fluoride)

	After final exam		
	Livionex	Crest Kids	Difference
Mean New Caries	0.93	1.19	-0.26
Std Dev	1.88	2.32	
# Subjects	27	32	
T Test Value			-0.33
df			55.4
P value (Two-Sided)			0.74
90% CI of the Difference	-1.00 < -0.26 < 0.47		
Mean Ratio (%) of Tooth Surfaces with Caries to Total Tooth Surfaces	1.10%	1.54%	-0.44%
Std Dev	2.26%	3.02%	
# Subjects	27	32	
T Test Value			-0.65
df			49.5
P value (Two-Sided)			0.52
90% CI of the Difference	-1.60% < -0.44% < 0.71%		

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