FINAL COMPREHENSIVE REPORT

I. Introduction

In the United States, dental caries is the leading chronic childhood disease (DHHS 2000). It is one of the most commonly overlooked and untreated illnesses (Newacheck et al. 2000). In the U.S., dental caries prevalence in the primary dentition of 2 to 11 year olds increased from 40% (1988-1994) to 42% (1999-2004) and moved even farther away from both Healthy People 2010 and 2020 objectives of reducing tooth decay. The burden is disproportionately borne by poor and minority children contributing to disparities (Dye et al. 2007). Furthermore, poor children suffer a significantly higher rate of tooth decay than their more affluent peers (Beltran-Aguilar et al. 2005). Billions of dollars in direct and indirect costs are spent each year to provide treatment and to deal with the consequences of this highly prevalent but preventable disease. While Best Practices have been identified including parental oral health education, promotion of tooth brushing, topical fluorides and dental sealants, they have a more limited impact in children with the highest tooth decay rates than in children with lower rates as research (Featherstone 2004, 2006) now shows that an antimicrobial agent is required.

This randomized controlled clinical trial addressed the prevention of dental caries (tooth decay) in inner-city school children using an antimicrobial agent, delivered via xylitol gummy bear snacks at school. Children were followed from Kindergarten to 2nd grade. Aim 1 was to determine if xylitol given during the kindergarten year reduces the incidence of caries in first permanent molars and other permanent teeth beyond the effects of oral health education, distribution of tooth brush and fluoridated tooth paste, fluoride varnish, and dental sealants. Aim 2 was to determine if the preventive effect of xylitol given during the Kindergarten year extends beyond the termination of its use, i.e. in second grade. This age group was chosen because prevention works best when the teeth are just erupting. Gummy bears (xylitol/placebo) were given 3 times daily during kindergarten, and within the supervised school environment. All enrolled children received the current best public health practices of oral health education, provision of tooth brush and fluoridated paste, fluoride varnish, and dental sealants as recommended by U.S. Preventive Services Taskforce and the Surgeon General.

Socio-demographic data was collected for all subjects. During the 30 month follow-up until second grade, all cases of dental caries were recorded every year.

II. Review of the Literature

The NIH Conference identifies sugarless and xylitol containing products as beneficial, in addition to recommended practices, i.e. oral health education, tooth brushing with fluoridated toothpaste, topical fluorides, and occlusal sealants. Xylitol products have received little study or application in the United States and thus are dramatically underused (Lynch and Milgrom 2003). Xylitol is a naturally occurring 5-carbon sugar polyol currently approved for use in foods, pharmaceuticals and oral health products in more than 35 countries. It is found naturally in various trees, fruits and vegetables and is an intermediate product of the glucose metabolic pathway in man and animals (Bar 1988). Although structurally dissimilar, it has approximately the same sweetness as sucrose or table sugar (Lindley, Birch et al. 1976) and an FDA-approved caloric content of 2.4 kcal/g compared with 4.0 kcal/g for sucrose. The most salient characteristic of xylitol is its extreme safety record. Xylitol has been FDA approved (Under FD& C Act Section 409, 172.395) as a dietary food additive since 1963 and has been used widely in the general market since the mid1970s. In 1983, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) reported xylitol to be a safe sweetener for foods. Currently, xylitol can

be found in the ingredients list of general market products such as gums, mints, candies, lozenges, soft drinks, toothpastes, and dietary food (Ly et al. 2006). To date, after nearly 30 years of xylitol product usage, there is no known reported case of major detrimental side effects related to the use of xylitol in food, gum, or syrup. Children can tolerate daily dose of 45g without developing side effects while the effective dosing range is several fold lower (Uhari, Kontiokari et al. 1998).

Numerous clinical studies have demonstrated a reduction in caries rates among young children who were exposed to xylitol daily. A field trial in Estonia used xylitol-containing candies among 10 year old school children showed a 35% to 60% caries reduction suggesting that candy may be as effective as chewing gum as a vehicle for the delivery of xylitol in caries prevention (Alanen et al. 2000). Similarly, The use of xylitol-containing chewing gum between meals has been demonstrated to reduce caries by 30% to 60% in Finnish teenagers (Isokangas, Alanen et al. 1988). Studies in Hungary, Belize, Estonia, Russia and the U.S. reported similar positive results (Scheinin, Pienihakkinen et al. 1985; Szoke, Pienihakkinen et al. 1985; Makinen, Bennett et al. 1995; Makinen, Makinen et al. 1996; Alanen, Isokangas et al. 2000). A recent systematic review (Antonio et al. 2011) of xylitol candies and lozenges favors a caries preventive effect.

The biological effects of xylitol are partly attributed to its interference with the metabolism and adherence of *S. mutans* and other cariogenic bacteria (Makinen 2000). Xylitol disrupts the energy production process of S. mutans leading to a futile energy consumption cycle causing cell death (Trahan 1991). Much evidence from controlled clinical studies of xylitol indicated that there is selective decrease in mutans streptococci level in plaque and saliva, possible decrease in plaque quantity, and xylitol aids the remineralization of enamel (Maguire and Rugg-Gunn 2003). A more recent study (Campus et al. 2009) reports reduction in plaque acidogenicity in children who chewed xylitol gum for 3 and 6 months.

Most European national dental associations as well as Canada and the U.S. endorse the use of xylitol as a preventive agent against dental caries. Finland has national programs promoting the use of xylitol chewing gum among all their children in an effort to reduce dental caries. Yet, xylitol-containing products are not widely promoted or used in the U.S. even when they have great potential to help control dental caries in high-risk populations.

The protective effect of xylitol is likely dependent on when teeth erupt. The Ylivieska (Finland) xylitol chewing gum study reported that xylitol gum reduced the DMFS scores not only during the intervention (Isokangas et al. 1988), but also after the discontinuation of the intervention in the 5 years after the termination of follow-up (Isokangas et al. 1993). Similarly, Hujoel et al. (1999) conducted a 5-year follow-up study after the termination of the Belize clinical trial where children, averaging 6 years of age at the start of the original study, chewed xylitol, xylitol/sorbitol, or sorbitol gum or no-gum for 2 years, and reported that xylitol gums reduced the caries risk 59% (RR, 0.41; $p < 0.0034$). Hujoel et al. concluded that xylitol chewing gum should be started at least one year before permanent teeth erupt to maximize for long-term caries preventive effects.

The current best practices of oral health education (Kay and Locker, 1998), tooth brushing with fluoridated tooth paste (Marinho et al. 2005), fluoride varnish (Helfenstein and Steiner 1994), and sealants (Truman et al. 2002) are each individually effective in reducing caries. However, Crall (2006) reports that no single modality is completely effective in eliminating caries, and the approach that giving some prevention is better than nothing for those without access to dental care is based on outdated evidence, inefficient use of resources, and suboptimal oral health for these children. Despite the use of current best practices, there is still disparity in caries rates

among poor children (Beltran-Aquilar et al. 2005). The caries balance model (Featherstone 2004, 2006) suggests that the balance between pathological factors (bacteria, frequency of cariogenic foods, salivary factors) and protective factors (fluoride, antibacterials such as xylitol, salivary flow and components) determine the progression of caries, and that increased bacterial challenge cannot be sufficiently overcome by fluoride alone. Milgrom et al. (2006) and Ly et al. (2006) indicate that the level of plaque mutans streptococci can be significantly reduced in as little as five weeks with daily xylitol use. A more recent study of Ly et al. (2008) shows that six week consumption of xylitol gummy bears (11.7 to 15.6 grams) showed reduction in plaque *S.* mutans levels. Thus adding xylitol as an antimicrobial agent can reduce the bacterial challenge and allow for eruption of healthier first permanent molars and other permanent teeth.

III. Study Design and Methods

A. Study Design: The study was designed as a two group, 30-month placebo-controlled double-blind class-room randomized clinical trial.

Each child received either xylitol or placebo (organic inulin fiber based gummy bear) gummy bears, 3 times per day during school hours for one academic year i.e. the Kindergarten year. Two pieces of gummy bear were given as snack after breakfast, lunch, and in the late afternoon totaling six pieces per day (xylitol: 7.8 grams; placebo fiber: 20 grams). The duration of 9 months of xylitol use was adequate to assess for caries preventive effects on permanent teeth since xylitol should be given prior to permanent teeth eruption. In the latter 18 months, no GB was given but all children continued to receive the remaining primary prevention components. Xylitol or placebo GB were given only within the supervised school environment and were not available to the children when not in school. The other primary prevention given to all the children regardless of group were: oral health education with tooth brush and tooth paste two times/year in KG, 1st, and once in 2nd grade; fluoride varnish application (initially 3M Vanish changed to 3M Cavity Shield, both containing 5% NaF) two times/year in KG, 1st and once in 2nd grade; and dental sealants on first permanent molars in 2nd grade.

B. Population Studied: The study sites were kindergarten classrooms in all five elementary schools of East Cleveland School District, Ohio. Cohorts of children were recruited in each of three school years (2007-2008, 2008-2009, 2009-2010). There were 10 to 12 classrooms in the five schools for each of the three years. The school district was 96% African American, with 94% of the children served by the federal reduced cost/free school lunch program, and English speaking parent/caregivers.

C. Sample Selection: To be eligible for the study, children needed to be healthy and free of severe stomach illnesses (ex. Crohn's disease, ulcerative colitis, Celiac disease, irritable bowel syndrome, etc.) or strict dietary restrictions (ex. Diabetes). Parents gave their written active informed consent. The University Hospitals Case Medical Center Institutional Review Board approved the study.

D. Instruments used: Dental data was collected in the school environment by trained and calibrated dental examiners using a portable dental chair. Self-administered socio-demographic information was collected from parent/caregiver at baseline. Other gummy bear consumption logs, school attendance, side effects and adverse events report, and dental referral follow-up were collected by trained outreach workers/study coordinator.

Dental exams included the collection of number of decayed, missing, or filled primary (dmfs/t) and permanent (DMFS/T) surfaces or teeth assessed in accordance to the International Caries Detection and Assessment System (ICDAS) at baseline, end of KG (time 1), beginning of 1st

grade (time 2), end of 1st grade (time 3), and exit exam in 2nd grade (time 4). Referrals were given for urgent/restorative needs. For the purposes of this study, an ICDAS severity score of 3 to 6 (localized enamel breakdown to extensive cavity) constituted the "d or D" portion of dmfs/DMFS.

E. Statistical techniques employed:

The analysis was based on the "intent to treat" model. The primary outcome for these analyses was caries progression from study entry (beginning of kindergarten) to four study follow-up exams: the end of kindergarten (t1), start of first grade (t2), end of first grade school year (t3), and December of the second-grade school year (t4). Caries progression was defined as number of surfaces exhibiting new d_{3-6}mfs as defined in Table 2 of Ismail *et al (2009)*. Separate analyses were performed for caries progression in permanent surfaces and in primary surfaces. Mean caries progression was compared between treatment groups. Confidence intervals and p-values were calculated using an optimally-weighted permutation test for cluster-randomized data (Braun and Feng, 2001). The permutation test procedures took into account the fact that the classrooms rather than children were the units of randomization, as well as the blocking used in the randomization (randomization was blocked within school and calendar-year cohort). Adjusted comparisons were also performed with the permutation tests using residuals from a negative binomial regression model adjusting for possible effects of caries severity at baseline, child gender, cohort and surface-years at risk. Caries severity at baseline was categorized into three groups, 0 dmfs, 1-5 dmfs, and 6 or greater dmfs. Surface-years at risk for a specific exam was calculated as the average of the number of surfaces at risk for new caries at the exam and at the baseline exam, multiplied by the amount of time between the two exams. The statistician performing the analyses was blinded to treatment assignment throughout. Calculations performed with the aid of SPSS version 16.0, and R version 2.7.1.

IV. Detailed Findings

Sample: Three cohorts of KG children were recruited from 5 elementary schools. A total of 672 caregivers were approached for participation, with 580 giving consent (86 % participation rate). Out of the 580 children, 18 were retained in KG, thus giving consents for two consecutive years, bringing the total number of recruited children to 562. The district wide low enrollment rates resulted in the study recruiting a third cohort to meet our original sample size goal. Classrooms were also downsized due to low enrollment in the school district.

Retention: Retention was challenging due to the transitional nature of the children going out of the school district. Approximately 85% were retained at the end of KG (n=476), 61% at the end of 1st grade (n=342), and 52% at the exit exam in 2nd grade (n=295).

Implementation of GB protocol: The gummy bear intervention was well received and there were no adverse events or major side effects from the intervention. A total of 17 children who had mild gastro-intestinal discomfort dropped out of the study. The majority of the children were compliant to the protocol of 6 GB consumption during the school day. But, because of the 9 month period of consumption, periodic incentives such as small gifts of pencils, stickers etc. were given to enhance compliance to the protocol. Attendance was used as a measure of the number of days of GB consumption. For example, if the child was absent any particular day, then they did not receive the intervention for that day. Excluding school holidays, absences, and other school activities, the actual mean GB consumption ranged between 5 to 6 months depending on the cohort. The consumption pattern was similar for the five schools.

Table 1: Baseline Characteristics of Children in Xylitol and Placebo Groups

	Treatment Assignment			
	Xylitol (n = 260)		**Placebo** (n = 266)	
Gender of child (N, %)				
Female	143	55%	137	52%
Male	117	45%	129	48%
Race/ethnicity of caregiver (N, %)				
African-American	192	85%	214	87%
Caucasian	4	2%	3	1%
Other	3	0%	8	3%
Not specified	26	12%	20	8%
School				
CA	47	18%	42	16%
CH	74	28%	78	29%
MF	45	17%	29	11%
PR	29	11%	54	20%
SP	65	25%	63	24%
Cohort (N, %)				
1st	91	35%	101	38%
2nd	91	35%	85	32%
3rd	78	30%	80	30%
Primary surfaces (mean, SD)				
number erupted	85.9	9.1	85.7	8.1
d_{3-6}	2.6	4.8	2.0	4.4
m	0.7	4.6	0.2	1.3
f	3.0	9.8	2.0	7.1
d_{3-6}mfs	6.3	11.8	4.3	8.7
Permanent surfaces (mean, SD)				
number erupted	8.8	12.6	9.7	13.7
D_{3-6}	0.0	0.1	0.0	0.1
M	0.0	0.0	0.0	0.0
F	0.0	0.0	0.0	0.1
D_{3-6}MFS	0.0	0.1	0.0	0.1
Overall caries burden (N, %)				
none (0 dmfs/DMFS)	112	43%	139	52%
moderate (1 - 5 dmfs/DMFS)	68	26%	66	25%
severe ($\geq$ 6* dmfs/DMFS)	80	31%	61	23%

* 6 is the 75% percentile of the cohort

Randomization: A total of 32 classrooms over the three KG years were randomized to treatment A (xylitol: 16 classrooms) and treatment B (placebo: 16 classrooms). A total of 260 children comprised the xylitol group and 266 children in the placebo group. The PI and all study staff delivering the gummy bear intervention, and dental examiners were blinded to the treatment assignment.

Baseline Characteristics: Table 1 shows that the two groups were similar in gender and ethnicity. Similar proportion of children was assigned to the xylitol and placebo groups in the five schools. The children assigned to the xylitol groups had significantly higher dmfs and severe caries burden. In both groups, very few permanent teeth had erupted at baseline, and thus DMFS was negligible.

Table 2: Mean new* DMFS by treatment group (permanent teeth)

	treatment assignment				Difference between groups			Adjusted** difference between groups			
	Xylitol		Placebo								
time point	N	Mean	N	Mean	Mean	95% CI		Mean	95% CI		p-value**
end of kindergarten	215	0.04	212	0.00	-0.03	-0.06	0.004	-0.04	-0.08	0.01	0.06
start of 1st grade	173	0.09	177	0.03	-0.06	-0.19	0.07	-0.08	-0.25	0.04	0.17
end of 1st grade	143	0.22	152	0.22	-0.01	-0.36	0.20	0.03	-0.28	0.23	0.86
middle of 2nd grade	122	0.38	140	0.48	0.10	-0.29	0.36	0.16	-0.16	0.43	0.25

* new since baseline exam (start of kindergarten)
** Adjust for child's gender, caries burden at study entry, school, and cohort

Table 3: Mean new* dmfs by treatment group (primary teeth)

	treatment assignment				Difference between groups			Adjusted** difference between groups			
	Xylitol		Placebo								
time point	N	Mean	N	Mean	Mean	95% CI		Mean	95% CI		p-value**
end of kindergarten	215	2.1	212	1.8	-0.3	-1.5	0.5	0.1	-1.1	0.7	0.88
start of 1st grade	173	2.7	177	2.7	0.0	-2.2	1.7	0.3	-1.7	1.6	0.77
end of 1st grade	143	3.4	152	3.2	-0.2	-1.9	0.9	-0.1	-1.5	1.2	0.91
middle of 2nd grade	122	5.0	139	4.0	-1.0	-3.4	0.1	-0.4	-2.5	0.8	0.45

* new since baseline exam (start of kindergarten)
** Adjust for child's gender, caries burden at study entry, surface-years at risk, and study cohort

Main Study Results: The xylitol and placebo treated groups had similar mean new DMFS at the end of KG, 1st grade, and at the exit exam in 2nd grade (Table 2) after adjusting for child's gender, caries burden at baseline, surface-years at risk, and study cohort. Caries progression in the permanent teeth of both groups was minimal. The mean new dmfs in the primary teeth were also similar between the xylitol and placebo groups after adjustment (Table 3). Caries progression in DMFS (Table 4) for the xylitol group at the exit exam was lower for males and those with severe caries.

Table 4: caries progression (mean new DMFS) by baseline characteristics and group

	Exam					
	End of KG		End of 1st grade		Exit exam - 2nd grade	
	Xylitol	placebo	xylitol	placebo	xylitol	placebo
Gender of child						
Female	0.04	0.01	0.25	0.34	0.47	0.49
Male	0.03	0.00	0.19	0.10	0.24	0.46
Race/ethnicity of caregiver						
African-American	0.05	0.00	0.22	0.25	0.44	0.55
Other	0.00	0.00	0.40	0.00	0.67	0.20
Not specified	0.00	0.00	0.30	0.14	0.25	0.27
Cohort						
2007-2008	0.04	0.01	0.21	0.16	0.21	0.08
2008-2009	0.05	0.00	0.25	0.18	0.43	0.37
2009-2010	0.02	0.00	0.21	0.33	0.48	1.07
School						
Caledonia	0.05	0.03	0.13	0.20	0.37	0.15
Chambers	0.02	0.00	0.30	0.21	0.50	0.55
Mayfair	0.00	0.00	0.17	0.05	0.10	0.29
Prospect	0.12	0.00	0.53	0.13	0.80	0.65
Superior	0.04	0.00	0.10	0.45	0.28	0.53
Overall caries burden						
none (0 dmfs/DMFS)	0.01	0.00	0.06	0.08	0.09	0.20
moderate (1 - 5 dmfs/DMFS)	0.02	0.00	0.40	0.23	0.50	0.35
severe ($\geq$ 6 dmfs/DMFS)	0.09	0.02	0.33	0.48	0.73	1.24

The important findings from the study are:

- Minorities are very willing to participate in clinical trials utilizing effective communication strategies and community outreach workers.
- The baseline caries rate in the KG children exceeds the national average of 28%.
- Only 19% of the parent/caregivers sought follow-up care for their children when they were given referrals based on baseline screening exams. Only 33% of children who

received urgent care actually did get follow-up care when examined at the subsequent dental exam.

- Our overall results indicate no differences between the xylitol and placebo groups in the mean new caries in permanent and primary teeth over time. There may be a beneficial effect of xylitol for those with severe caries which needs to be explored further with a larger sample size. Caries progression in the permanent teeth was minimal for both groups.

V. Discussion and Interpretation of Findings

Conclusions: Our hypothesis that xylitol will have short-term (during the period of use in KG), and long-term (in 2nd grade) effects on caries prevention in permanent teeth was not supported by our data. Xylitol did not add any additional benefit to the other simultaneous prevention (oral health education, fluoride varnish, dental sealants) that was also given. But, there may be a beneficial effect of xylitol long-term for children with severe caries. This will be explored further with additional analyses. Overall, the multi-modality approach to prevention was effective for prevention and progression of permanent caries.

Study limitations: Several limitations may have precluded this study from observing a xylitol effect. First, retention was a huge challenge in this school district since nearly half the children had moved out of the school district by the time of the exit exam in 2nd grade. This was unanticipated at the onset of the study. It is likely that children who moved could have had a different caries status compared to the children who were retained in the study. The power calculation indicated that a total of 300 children in each group were essential to observe a xylitol effect. Second, outreach workers at each school were responsible for distribution of the GB's in the classroom. It is likely that at times certain doses were missed or children did not comply in eating the 6 GB's/day. The research staff followed best practices for enhancing compliance through periodic incentives for children and teachers, and weekly random monitoring of outreach workers in the distribution of GB's. Third, other recommended prevention such as oral health education with tooth brush and paste, and fluoride varnish two times/year that were given simultaneously may have masked the xylitol effect. Fourth, the chewing of placebo (fiber) GB's may have been responsible for increasing saliva stimulation and buffering capacity that may have been beneficial for caries prevention.

Comparison with other findings: Our results are in contrast to previous clinical studies (Alanen et al. 2000; Honkala et al. 2006) that suggest a caries preventive effect of xylitol candies and lozenges. In these prior studies, xylitol intervention was given for 2 to 3 years in older children (>= 10 years) compared to the 9 month intervention and younger children in our study. Also, a recent systematic review (Antonio et al. 2011) indicated that these studies showed high risk of bias due to lack of randomization of subjects. Other previous xylitol studies may not be directly comparable to ours due to the use of chewing gums, smaller dosage of xylitol, and the use of other polyols with xylitol.

Application to MCH Health Care Delivery Systems: The study findings are applicable to MCHB strategic research issues that address health disparities and improvement of child health. A multi-modality approach to caries prevention is recommended for high risk children.

Policy Implication: Our study has shown that a multi-modality approach to prevention is beneficial in reducing permanent caries incidence. While our study did not show a beneficial effect of xylitol due to various limitations, it may still be beneficial for high risk children (based on

prior literature and its mechanism of action on *S*. mutans) if the logistics of delivery can be improved. Thus, better vehicles of delivery with reduced frequency would promote xylitol use in various settings.

Suggestions for further research: More clinical studies are needed to test the effectiveness of xylitol by including some surrogate *S*.mutans outcomes that can be tested in a shorter time frame. Our study is not definitive due to the challenges of retention that we encountered during its implementation.

VI. List of products

Published Manuscripts:

1. Nelson S, Eggertsson H, Powell B, Mandaleris J, Ntragatakis M, Richardson T, Ferretti G. Calibration of dental examiners in the ICDAS criteria for a caries prevention community trial. Community Dent Health. 2011 Sep;28(3):238-42. PMID: 21916361
2. Nelson S, Milgrom P. Recruitment of Minority School Children into a Randomized Clinical Trial of Tooth Decay Prevention. Contemp Clin Trials. 2012 Jan;33(1):60-6. Epub 2011 Oct 1. PMID: 21986390
3. Nelson S, Mandelaris J, Heima M, Ferretti G, Spiekerman C, Milgrom P. School screening and parental reminders in increasing dental care for children in need: a retrospective cohort study. J Public Health Dentistry 2011 doi: 10.1111/j.1752-7325.2011.00282.x

Published Abstracts:

1. Lee W, Asaad R, Nelson S. Retention issues in urban school-based randomized trials. AADR Oral Health Disparities Fall Symposium November 2011 #35.
2. Nelson S, Ly K, Milgrom P, Spiekerman C, Richardson T, Ntragatakis M, Ferretti G, Powell B, Lombardi G. School-based xylitol gummy bear for caries prevention trial: Baseline findings. IADR Miami April 2009 #2815.
3. Gerstenmaier JH, Ntragatakis M, Richardson T, Nelson S, Ferretti G. Oral health education of Kindergarten children from urban school district. IADR Toronto July 2008 #2440.

Future manuscript submission includes reporting of the final results of this project. Dissemination of findings have/will been done through local/national/international meetings and publications in peer-reviewed journals. Findings are also disseminated through the School administrators, school principals and teachers. Additionally, yearly newsletters were sent to study participants. The final results of the project will be disseminated to the school community and the parent/caregiver participants through a newsletter. Community outreach workers were trained to carry important oral health messages to the children and parent/caregivers.

One important finding from our study that only 19% of the caregivers followed up with appropriate further dental care for their children instigated our thinking that family level interventions are essential in addition to child level prevention. Thus, these findings was instrumental in helping us obtain a two year developmental NIDCR grant (R34 DE022262-01, 9/15/2011 – 8/31/2013) to develop a new referral method and intervene with the families to change their illness perception and provide resources to seek timely care. The R34 findings will be used to submit a U01 clinical trial grant to compare the effectiveness of the new referral method with the existing standard referral recruiting children from the same school district.

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