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Changes in Caries Risk in a Practice-Based Randomized Controlled Trial

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Abstract

To demonstrate that Caries Management by Risk Assessment (CAMBRA) can be successfully implemented in dental practice, 30 dentists were recruited to perform a 2-y CAMBRA trial. Twenty-one dentists (18 private practices, 3 community clinics) participated in a randomized, controlled, parallel-arm, double-blind clinical trial with individual-level assignment of 460 participants to standard of care (control) versus active CAMBRA treatment (intervention). Control or active antimicrobial and remineralizing agents were dispensed at baseline and 6-, 12-, 18-, and 24-mo recall visits according to risk level and assigned treatment arm. Primary outcome measure was dentist-determined caries risk level at recall. Among initially high-risk participants, secondary outcomes were recorded disease indicators. Generalized estimating equations were used to fit log-linear models for each outcome while accounting for repeated measurements. At 24 mo, follow-up rates were 34.3% for high-risk participants (32.1% intervention, 37.1% control) and 44.2% for low-risk participants (38.7% intervention, 49.5% control). Among 242 participants classified as high caries risk at baseline (137 intervention, 105 control), a lower percentage of participants remained at high risk in the intervention group (statistically significant at all time points). At 24 mo, 25% in the intervention group and 54% in the control group remained at high risk ($P = 0.003$). Among 192 participants initially classified as low risk (93 intervention, 99 control), most participants remained at low risk. At 24 mo, 89% in the intervention group and 71% in the control group were low caries risk ($P = 0.18$). The percentage of initially high-risk participants with recorded disease indicators decreased over time in both intervention and control groups, being always lower for the intervention group (statistically significant at the 12- and 18-mo time point). In this practice-based clinical trial, a significantly greater percentage of high-caries-risk participants were classified at a lower risk level after CAMBRA preventive therapies were provided. Most participants initially assessed at low caries risk stayed at low risk (ClinicalTrials.gov NCT01176396).

Keywords: dental caries, Caries Management by Risk Assessment (CAMBRA), Practice-Based Research Network (PBRN), caries risk assessment, disease indicators, caries prevention

Background

Minimally invasive treatment concepts (Mertz-Fairhurst et al. 1998; Tassery et al. 2013; Walsh and Brostek 2013) are increasingly accepted by dental practitioners. Under these concepts, invasive restorative treatments are delayed and performed at more advanced caries lesion stages (Vidnes-Kopperud et al. 2011; Doméjean et al. 2015; Rechmann et al. 2016).

The decision to postpone operative treatment depends on each patient's caries risk. Consequently, assigning individualized preventive, nonoperative treatment to manage caries becomes necessary. The Caries Management by Risk Assessment (CAMBRA) philosophy was developed in California following 2 consensus conferences (Featherstone 2003; Featherstone et al. 2007). The first CAMBRA randomized, controlled clinical trial at the University of California at San Francisco (UCSF) showed therapeutic intervention that included a combination of antibacterial and fluoride products that significantly reduced patient bacterial load. The study also demonstrated reduced 2-y caries increment in initially high caries risk patients provided with the therapeutic intervention (Featherstone et al. 2012).

Several CAMBRA outcome studies have been published. The utility of the caries risk assessment (CRA) component of CAMBRA was supported by 2 prediction studies (Doméjean-Orliaguet et al. 2006; Doméjean et al. 2011). In the latter, among 2,571 patients categorized at baseline as low, moderate, high, or extreme caries risk, the occurrence of new visually cavitated or radiographic carious lesions was 24%, 39%, 69%, and 88%, respectively, at follow-up visits 1.5 to 3 y later (Doméjean et al. 2011). The multicomponent CAMBRA CRA was recently confirmed as strongly associated with future treatment needs (Chaffee et al. 2015).

The original UCSF-CAMBRA trial occurred in a structured university dental school setting (Featherstone et al. 2012). The CRA prediction papers were also based in dental school settings. To demonstrate successful CAMBRA implementation

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A supplemental appendix to this article is available online.

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in private practices, dentists in the San Francisco Bay Area were recruited to participate in a Practice-Based Research Network (PBRN) study. The hypothesis to be tested was that caries management based on caries risk level significantly reduces the need for caries restorative treatment over 2 y compared to generally accepted standard of care. The primary outcome measure was caries increment. Change in caries risk level was a secondary outcome.

The goal of the CAMBRA-PBRN study was to recruit 30 dentists to perform a 2-y randomized, controlled, double-blind study involving approximately 30 patients per dentist. After initial screening, treatment of all cavitated caries lesions, and assessment of caries risk, participants were randomly assigned to either an active preventive intervention or a "standard-of-care" control treatment. Newly formed caries lesions and changes in caries risk level were monitored. The present paper reports on the outcome "change in caries risk level."

Materials and Methods

Dentist Recruitment, Training, and Calibration

Through advertisements and personal phone calls, San Francisco Bay Area dentists were invited to attend information meetings about the CAMBRA-PBRN study. The UCSF Institutional Review Board (IRB) approved the study (IRB 10-02153) and prestudy dentist calibration (IRB 10-04804). The study was registered at ClinicalTrials.gov (ID: NCT01176396). This practice-based trial was a double-blind (subject, investigator), parallel-arm clinical study with participant-level assignment within each office to standard-of-care treatment (control) or active preventive treatment (intervention).

During 1-d information sessions organized by the California Dental Association (CDA), the study design, expected dentist involvement, and participation requirements were explained. Thirty dentists (13 female, 17 male) enrolled. Three dentists were employed at 3 Federally Qualified Health Centers (FQHCs), and 27 owned dental offices.

Dentists were required to attend 1 training meeting and 1 calibration workshop, each offered on multiple dates and attended by 3 to 8 dentists per session. The goal of calibration was to minimize interexaminer variability in data gathering, including CRA, carious lesions classification, and recording existing restorations. The attendees were trained and standardized in examining decayed, missing, and filled surfaces (DMFS) (Klein et al. 1938; World Health Organization 2013) and International Caries Detection and Assessment System (ICDAS) criteria for noncavitated lesions (Pitts 2004). The examination occurred after the teeth were carefully cleaned (dental prophylaxis). Dentists performed a visual exam (no tactile probing) using loupes with ×2 magnification. All dentists achieved interexaminer κ values of >0.75 in comparison to a gold-standard examiner.

Patient Inclusion and Exclusion Criteria

Patients were required to meet the following inclusion criteria:

- new patients (new to CAMBRA);
- ≥12 y and not older than 65 y;
- able to give informed consent in English;
- unlikely to move from the area within 2.5 y for work, educational, or personal reasons (determined by residential history and questioning);
- willing to participate regardless of group assignment;
- willing to comply with all study procedures and protocol;
- ≥16 permanent teeth;
- completed restorative treatment of cavitated lesions before study entry.

Exclusion criteria were the following:

- not willing to have dental radiographs taken;
- significant past or current medical conditions that might affect oral health or oral flora (i.e., diabetes, human immunodeficiency virus, heart conditions requiring antibiotic prophylaxis);
- medication use that might affect the oral flora or salivary flow (e.g., antibiotic use in the past 3 mo, drugs associated with dry mouth/xerostomia);
- root caries at enrollment;
- periodontal disease requiring surgery, chemotherapeutic agents, or frequent prophylaxis;
- another household member participating in the study (to prevent sharing rinses, etc.);
- drug or alcohol addiction or other conditions that might decrease the likelihood of adhering to study protocol;
- missed screening visit without cancellation or rescheduling;
- rescheduled screening visit more than once;
- subjects with extreme high caries risk (due to ethical reasons);
- sensitive to chlorhexidine or the ethyl alcohol vehicle in chlorhexidine.

Participants or parents gave informed written consent ahead of enrollment and signed a Health Insurance Portability and Accountability Act (HIPAA) form, "Authorization for Release of Personal Health Information and Use of Personally Unidentified Study Data for Research."

Study Offices

Of the 30 calibrated dentists, 21 (11 female and 10 male) recruited patients for the study. Eighteen dentists were office owners and 3 were FQHC employees.

DMFS Charting

For each participant, the DMFS was recorded in Denticon, a web-based dental charting program (Planet DDS). The program also provided secure data storage.

CRA

CRA was performed following completion of restorative treatment for all cavitated lesions and/or other treatment needs. To

Table 1. Caries Risk Levels and Dispensed Products for the Intervention and the Control Group Patients.

	Dispensed Products	
Caries Risk Level	Intervention Group	Control Group
Low caries risk	Crest cavity protection (P&G) (1,100 ppm F), 2×/d	Crest cavity protection (P&G) (1,100 ppm F), 2×/d
Moderate caries risk	Crest cavity protection (P&G) (1,100 ppm F), 2×/d	Crest cavity protection (P&G) (1,100 ppm F), 2×/d
	Ortho wash rinse (3M ESPE) (0.05% F), daily	Crest Scope rinse (P&G) (mint taste), daily
	Xylitol candies (Epic) (8 g), 4×/d	Sorbitol candies (Epic) (8 g), 4×/d
High caries risk	Clinpro 5000 (3M ESPE) (5,000 ppm F toothpaste)	Crest cavity protection (P&G) (1,100 ppm F), 2×/d
	Peridex (3M ESPE) chlorhexidine gluconate (0.12%) rinse 1/d for 1 wk, every month until the next periodic oral exam, then reassess	Crest Scope rinse (P&G) (mint taste), daily
	Xylitol candies (Epic) (8 g), 4×/d	Sorbitol candies (Epic) (8 g), 4×/d
	Vanish (3M ESPE) F-varnish	Placebo varnish (3M ESPE)

reduce variation in assessing risk levels, each participant's caries risk was assessed using a computer algorithm. The system had been developed at UCSF to aid private practitioners (MyCAMBRA App; Apple AppStore) (Rechmann and Featherstone 2014). The digital system requires input of clinical findings and answers to questions on the CDA's CRA form (Featherstone et al. 2003; Featherstone et al. 2007). The MyCAMBRA App was developed based on the CRA procedures previously published (Featherstone et al. 2007). For the CAMBRA-PBRN study, this risk assessment system was integrated into the Denticon charting program. Disease indicators, risk factors, protective factors, and caries risk levels were recorded for each participant visit.

The first baseline CRA performed in the CAMBRA-PBRN study occurred on May 16, 2012. The last baseline CRA was performed on June 26, 2015, and the final 24-mo follow-up CRA was completed on December 29, 2016.

Treatment Group Randomization

Separately for each risk level (low, moderate, high), a printed randomization list was provided to every office. Each row on each list was marked with a black or white mark with a 1:1 allocation ratio. A random number generator determined the order of the colored marks (GraphPad Software). A participant identified with a specific risk level was recorded in the first available empty row of that list (e.g., first participant at high risk, first line of the high-risk list). This ensured that each participant was randomly assigned to the "black" or "white" treatment group, with the nature of each group concealed from provider dentists.

Eligibility for Analysis

Participants were regarded as eligible for data evaluation if a baseline CRA was performed and group assignment ("black" or "white") was recorded in the participant's computer chart.

Treatment Products and Blinding

Table 1 describes the treatment recommendations and products according to risk level and assigned treatment group. Intervention group products and recommendations were based on CAMBRA guidelines (Featherstone et al. 2007; Jenson et al. 2007).

All dispensed products were concealed with black or white labels so that participants or the dispensing person could not identify brand names or contents. User instructions were printed on the labels. According to the group assignment, a black/white product bag was given to the participant containing all products recommended for the specific risk level. The color-coding ensured that dentists, office staff, dental hygienists, and participants were blinded to group assignment. Products supplied were sufficient for 6 mo. Participants were instructed to contact the dental office if they required additional assigned products.

Recall Intervals

Participants were scheduled for a recall examination at 6, 12, 18, and 24 mo after baseline. Participants were instructed to return to the office if any adverse dental event occurred.

At the beginning of the study, 4 bitewing radiographs were performed for each participant. For low- and moderate-risk participants, bitewings were repeated every 12 mo; for high risk, every 6 mo. Every 6 mo, a dental prophylaxis with oral hygiene instructions was scheduled.

Compliance

Each product bag included laminated, detailed instruction for home use. Participants were told to place the instruction sheet at the bathroom mirror. Dental offices contacted each high-caries-risk participant the week prior to a new month and reminded participants to use their assigned rinse for the first week of the month (1-min rinse, 60 min after brushing teeth each evening). Each office was reminded via telephone call from the UCSF study coordinator (B.M.T.R.) to place those reminder phone calls to the participating patients.

Outcome Measures

The primary outcome measure was assigned CRA level at recall. Among participants classified as high risk at baseline, the main outcome was assignment to either low or moderate

risk at follow-up (i.e., no longer high risk). Among participants initially classified as low risk, the main outcome was assignment to either moderate or high risk at follow-up (i.e., no longer low risk). Among initially high-risk participants, secondary outcomes were derived from clinical items in the CRA form: presence of carious lesions into dentin, proximal enamel lesions evidence on radiograph, active white spot lesions, restorations within the prior year, or a composite variable defined as having any of those 4 clinical findings.

Statistical Power

Study recruitment was planned for 900 patients (30 dentists × 30 patients/dentist), anticipating 88% power among initially high-risk patients to detect a relative risk for incidence of any new decay or restorations of 0.5 between intervention and control groups at 24 mo, assuming 20% decay in the intervention group, a design effect of 1.5 for intraoffice clustering, 25% loss to follow-up, 2-tailed $\alpha = 0.05$, and 50% of the total sample being high risk at baseline. For the present analysis, the recruited 460 participants would provide 93% power to observe conversion of initially high-risk participants to low or moderate risk at 50% (intervention) versus 20% (control) and 65% power to compare 40% (intervention) versus 20% (control), under the same assumptions.

Data Analysis

Baseline sociodemographic variables (i.e., age, sex) and baseline CRA level were compared according to treatment group using pairwise hypothesis tests (i.e., *t* test, χ^2). For main and secondary outcomes (i.e., CRA risk level and clinical items) and separately for initially high- and low-risk participants, generalized estimating equations (GEEs) were used to fit log-linear models for each outcome while accounting for repeated measurements within individuals and dental offices (exchangeable correlation structure). Global differences between originally assigned treatment groups over the follow-up period were obtained from GEE models including only group assignment as the independent variable; differences at each follow-up visit were obtained from models including group × visit interaction terms. Models were used to calculate cluster-adjusted relative risks, 95% confidence intervals, and *P* values. Three sensitivity analyses were conducted to assess robustness to assumptions regarding missing observations, including last observation carried forward and single and multiple imputation (Appendix). The data analyst remained masked to the nature of the treatment groups until analyses were complete.

Results

Of the 30 calibrated dentists, only 21 (11 female and 10 male) actively recruited patients. Nine offices did not recruit any patients despite a 1-d in-office training and being provided with all necessary study material. In addition, all data from 1 office were excluded (19 participants) because the office did not follow recruitment, recall, and data collection instructions. The remaining 20 dentists, representing 17 office owners and 3 FQHC employees, enrolled 460 eligible participants. Each office enrolled a mean of 23.4 ± 16.5 participants (range, 2 to 55).

At baseline, 192 participants were classified as low, 26 as moderate, and 242 as high caries risk. Of the high-risk participants, 137 were randomly assigned to the intervention and 105 to the control group. Of low-caries-risk participants, 93 were randomly assigned to the intervention and 99 to the control group (Fig. 1). At baseline, the intervention group and the control group were not statistically significantly different in terms of mean age (37 y intervention; 35 y control; $P = 0.28$; data available for 362 participants) and sex (69% female intervention; 68% female control; $P = 0.95$). By chance, randomized allocation resulted in a higher percentage of high-caries-risk participants at baseline in the intervention group (57% intervention; 48% control; $P = 0.05$).

Important Adverse Events or Side Effects

No adverse events, side effects, or harm were reported.

High Caries Risk

Table 2 depicts the number and percentage of participants initially classified as high caries risk who were still classified as high risk at each follow-up visit, in total and by treatment group assignment. For the intervention group, the follow-up rate was 58.4% at 6 mo, 50.4% at 12 mo, at 39.4% 18 mo, and 32.1% at 24 mo, while for the control group, the follow-up rates were 54.3%, 44.8%, 39%, and 37.1%, respectively. In total, 151 initially high-risk participants contributed at least 1 follow-up visit: 85 (62.0%) in the intervention group and 66 (62.9%) in the control group. Figure 2A shows that for participants assessed as high caries risk at baseline, the percentage of participants who remained high risk over time was lower in the intervention group than in the control group, reaching just 25% in the intervention group at the 24-mo recall. The percentage of high-caries-risk participants was also reduced in the control group. For all time points, differences between the 2 groups were statistically significant (Table 2). The statistically significant difference between the intervention and control groups persisted in sensitivity analyses using different missing data approaches (Appendix).

Low Caries Risk

Table 2 reports the number and percentage of participants initially classified as low caries risk who were later classified as low or moderate risk at each follow-up visit, in total and by treatment group. For the intervention group, the follow-up rate was 68.8% at 6 mo, 60.2% at 12 mo, 57% at 18 mo, and 38.7% at 24 mo, while for the control group, the follow-up rates were 72.7%, 70.7%, 59.6%, and 49.5%, respectively. In total, 154 initially low-risk participants contributed at least 1 follow-up visit: 73 (78.5%) in the intervention group and 81 (81.8%) in

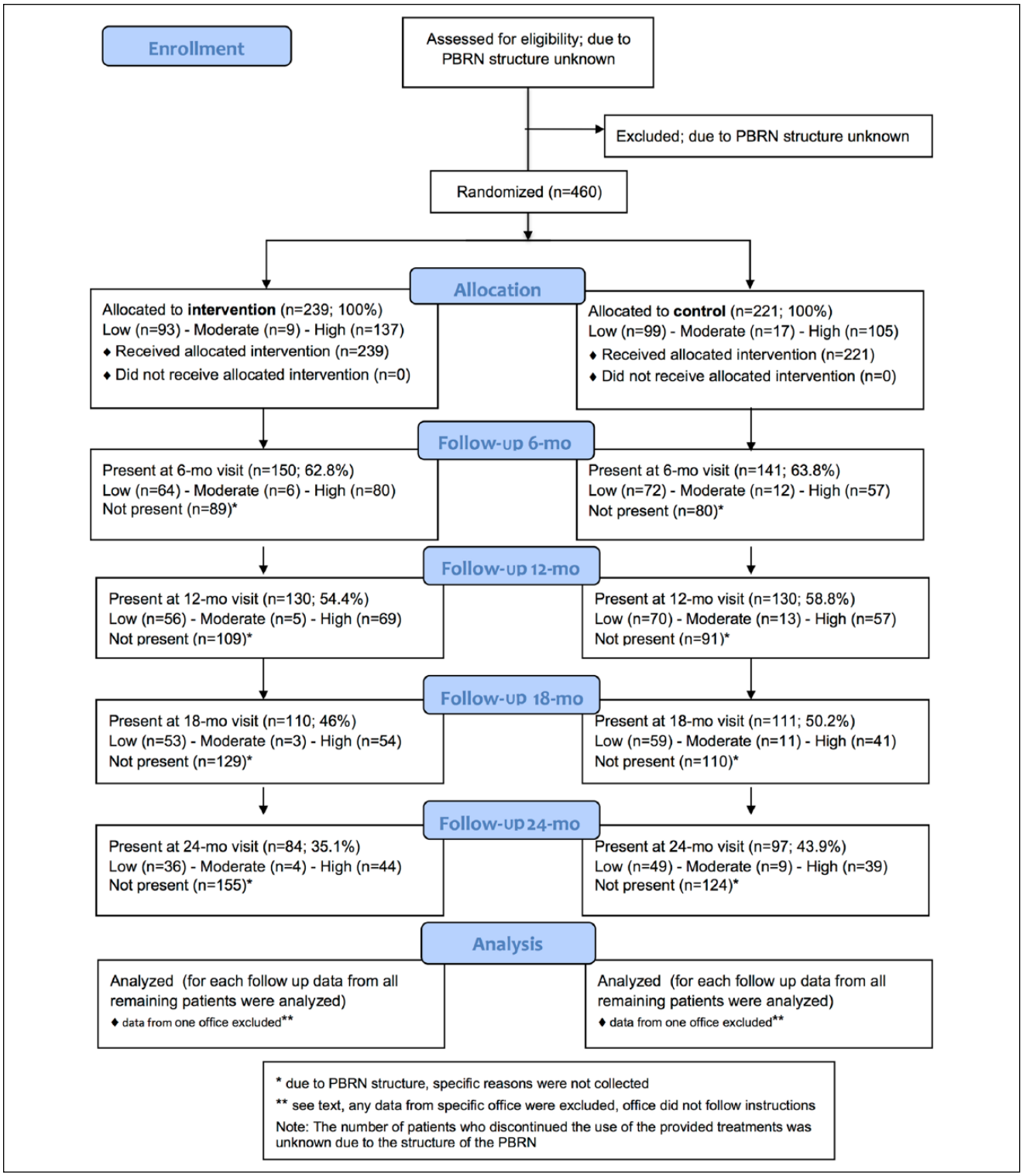

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flowchart with patients followed from baseline and at each follow-up visit, by group status. PBRN, Practice-Based Research Network.

the control group. Figure 2B shows the change in risk level for participants who were assessed at baseline as low caries risk. A small percentage of these participants converted to high caries risk over time. At the 18-mo recall, 3.9% of the intervention group and 18.0% of the control group were classified as moderate or high caries risk ($P = 0.05$) (Table 2). At no other time

Table 2. Caries Risk Category at Baseline and Follow-up Visits, according to Baseline Caries Risk and Treatment Group Assignment.

	Total		Intervention Group		Control Group			
Visit	*n*	High Risk, *n* (%)	*n*	High Risk, *n* (%)	*n*	High Risk, *n* (%)	*P* Value[a]	Risk Ratio (95% CI)[a]
High caries risk at baseline								
Baseline	242	242 (100)	137	137 (100)	105	105 (100)	<0.01[b]	0.67 (0.53–0.84)[b]
6 mo	137	92 (67.2)	80	49 (61.3)	57	43 (75.4)	0.03	0.78 (0.62–0.97)
12 mo	116	60 (51.7)	69	30 (43.5)	47	30 (63.8)	0.02	0.67 (0.48–0.95)
18 mo	95	32 (33.7)	54	13 (24.1)	41	19 (46.3)	0.02	0.52 (0.30–0.91)
24 mo	83	32 (38.6)	44	11 (25.0)	39	21 (53.8)	<0.01	0.42 (0.23–0.74)
Visit	*n*	Moderate or High Risk, *n* (%)	*n*	Moderate or High Risk, *n* (%)	*n*	Moderate or High Risk, *n* (%)	*P* Value[a]	Risk Ratio (95% CI)[a]
Low caries risk at baseline								
Baseline	192	0 (0)	93	0 (0)	99	0 (0)	0.02[b]	0.43 (0.22–0.86)[b]
6 mo	136	12 (8.8)	64	5 (7.8)	72	7 (9.7)	0.70	0.81 (0.28–2.38)
12 mo	126	14 (11.1)	56	3 (5.4)	70	11 (15.7)	0.08	0.32 (0.09–1.13)
18 mo	112	11 (9.8)	53	2 (3.8)	59	9 (15.3)	0.05	0.22 (0.05–1.00)
24 mo	85	15 (17.7)	36	4 (11.1)	49	11 (22.5)	0.18	0.47 (0.16–1.42)

For patients classified at baseline as high caries risk (upper rows) or low caries risk (lower rows), the number and percentage of patients who remained high risk (upper rows) or changing to moderate or high risk (lower rows) are shown according to assigned treatment group.
CI, confidence interval.
[a]Comparing intervention to control group, adjusted for repeated measures in generalized estimating equation (GEE) models.
[b]Global contrast over all postbaseline study visits in GEE models (i.e., not time point specific).

point was the difference between intervention and control statistically significant, but averaged over the total study period, the percentage of participants classified as moderate or high risk was lower in the intervention group ($P = 0.03$) (Table 2).

Clinical Outcomes: Disease Indicators

Figure 2C represents the percentage of participants demonstrating newly registered disease indicators: radiographic cavities into dentin, proximal enamel lesions, restorations due to caries in the past year, and active white spot lesions at each recall time point. The percentage of newly developed diseases indicators decreased over time in both study groups. At all time points, the percentage of participants with newly registered disease indicators was lower for participants in the intervention group than for those in the control group. For the 12- and 18-mo recall, the differences were statistically significant: 46% for the intervention group and 64% for the control group at 12 mo and 53% and 31%, respectively, at 18 mo ($P = 0.04$) (Table 3).

Discussion

To study whether CAMBRA can be successfully implemented outside a structured university setting (Featherstone et al. 2012), a PBRN was created in the San Francisco Bay Area. Thirty dentists were enrolled to perform a 2-y, randomized, controlled, double-blind clinical CAMBRA trial in their practices. The dentists were trained and calibrated to assess caries risk and score the conventional DMFS index.

To minimize previously observed deficiencies in CRA consistency among dentists, each participating dentist was trained to assign caries risk levels. A 2014 study asked university clinical instructors to complete CRA forms for simulated patients (Rechmann and Featherstone 2014) and showed that the reliability to assign caries risk levels correctly was only moderate. Twenty percent of the depicted high caries risk cases were underestimated at lower caries risk. Goolsby and Young both found similar patterns among tested faculty (Goolsby et al. 2016; Young et al. 2017).

Overestimating the caries risk may increase preventive therapy but is not economical; in contrast, underrating the caries risk might have serious consequences. Doméjean et al. (2011) discovered in a follow-up study that 23.6% of 2,571 patients assessed as low caries risk at baseline had developed new cavities 16 mo later. Plausibly, many of these patients were wrongly assessed as low caries risk.

To prevent such misjudgments from influencing the present study, an electronic system to assign caries risk levels was developed. It was modeled after the way the gold standard and 2 experienced clinical teachers had assigned caries risk in the UCSF quality assurance study (Rechmann and Featherstone 2014). This system was integrated in the dental charting program provided to all study dentists.

The previous university clinic-based UCSF-CAMBRA trial included only high caries risk patients (Featherstone et al. 2012). Interventions resulted in a significantly lower percentage of participants at high risk and high/medium bacterial challenge from baseline to the point restorations were completed (Featherstone et al. 2012). While the bacterial challenge stayed low for the intervention group over 24 mo, the overall risk level increased at 24 mo, reaching the baseline level of the controls. In the intervention group, 50% to 70% of participants

stayed at high caries risk, while in the control, 70% to 90% resided at this risk level over time. In contrast, in the CAMBRA-PBRN study, 75% of the participants in the intervention group and 47% of the control group showed a reduced caries risk at the end of the study. At all recall time points, differences between control and intervention group were statistically significant.

The percentage of initially high-risk participants remaining at high risk during subsequent visits was much lower in the present CAMBRA-PBRN than in the UCSF-CAMBRA trial. The reasons may be multifaceted. In the UCSF-CAMBRA study, 0.12% chlorhexidine plus over-the-counter (OTC) fluoride rinse and OTC fluoride toothpaste (1,100 ppm F-paste) served as intervention products. High-caries-risk participants in the CAMBRA-PBRN study received a combination of prescription 5,000 ppm F-paste, chlorhexidine rinse, xylitol mints, and fluoride varnish. As in the UCSF-CAMBRA study, the products were provided for the intervention group, but in contrast to the UCSF-CAMBRA study, where the control group "continued their usual products," in the present study, the standard-of-care products were also provided to the control group, likely contributing to the reduction in risk for the control group over time. The control products likely enhanced saliva flow (sorbitol candies) and might have had bactericidal effects (cetylpyridinium chloride rinse). Consequently, the risk level of participants in the control group was more dramatically reduced over time than in the UCSF-CAMBRA study.

In addition, for participants at high caries risk, the occurrence of newly recorded disease indicators decreased for both treatment groups. At all time points, the percentage of newly developed disease indicators was lower for participants in the intervention group than for those in the control group. A reduced number of newly developed disease indicators clearly demonstrates a reduction in the disease "caries" expressed by radiographic cavities into dentin, proximal enamel lesions, restorations due to caries in the past year, and active white spot lesions. Since the disease indicators strongly determine the caries risk level, the observed reduction in the percentage of participants with high caries risk and the decreased percentage of newly developed disease indicators coincided.

The CAMBRA-PBRN study also enrolled participants at moderate or low caries risk. At baseline, too few participants (5.7%) were classified at moderate risk to study as a separate category. As expected, a small percentage of low-caries-risk participants showed an increased caries risk over time; however, the observed increase in risk level at 24 mo could result from possible changes in participant habits or other risk or protective factors. Differences between intervention and control groups were not consistently statistically significant but were statistically significantly different at the 18-mo visit, despite both groups receiving the same prevention products.

Study Limitations

Study attrition was high (65%), despite incentivizing dentists and providing products for participants in both study groups.

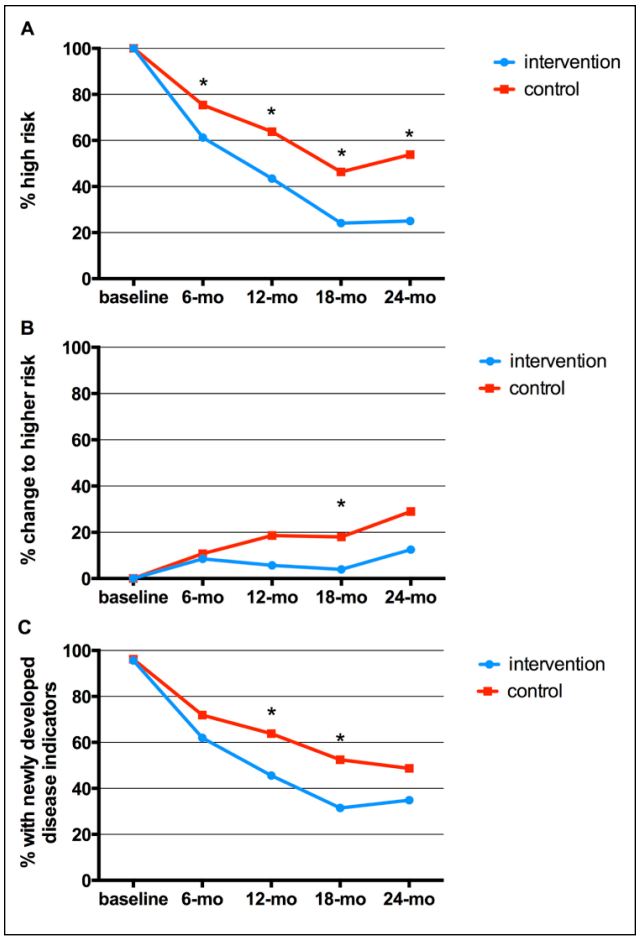

Figure 2. Change in caries risk levels and development of new disease indicators. (**A**) Among patients classified as high caries risk at baseline, percentage of patients staying at high risk over time for intervention and control group. (**B**) Among patients classified as low caries risk at baseline, percentage of patients with increased risk level over time for intervention and control group. (**C**) Patients with initial high risk, percentage developing any of the 4 clinical outcomes/disease indicators (cavities on radiographic into dentin, proximal enamel lesions on radiographs, active white spot lesions on smooth surfaces, restorations within prior year). *Percentages statistically significant different (cluster-adjusted $P < 0.05$).

Attrition was comparable to the UCSF-CAMBRA trial (53%). However, it cannot be ruled out that losses to follow-up partly contributed to the observed declines in risk level at each subsequent recall visit, although there was unlikely to be a differential bias between intervention and control groups, for which attrition percentages were nearly equal.

The CAMBRA-PBRN study also showed some major challenges that a practice-based clinical trial is confronted with. A serious amount of time and major financial resources were spent training and calibrating 30 dental practitioners, who owned private dental offices or were employees of FQHCs. Nevertheless, despite all efforts, only 21 of the 30 dentists really attempted to recruit patients into the study. This was impossible to predict, since all the dentists willingly agreed to participate. In addition, the very wide range of the number of

Table 3. Clinical Disease Indicators at Baseline and Follow-up Visits among Initially High-Risk Patients, according to Baseline Caries Risk and Treatment Group Assignment.

	Total		Intervention Group		Control Group			
Clinical Outcome/Visit	*n*	With Outcome, *n* (%)	*n*	With Outcome, *n* (%)	*n*	With Outcome, *n* (%)	*P* Value[a]	Risk Ratio (95% CI)[a]
Cavities on radiograph into dentin								
Baseline	242	42 (17.4)	137	24 (17.5)	105	18 (17.1)	0.33[b]	0.71 (0.36–1.42)[b]
6 mo	136	9 (6.6)	79	5 (6.3)	57	4 (7.0)	0.86	0.89 (0.25–3.15)
12 mo	115	9 (7.8)	68	7 (10.3)	47	2 (4.3)	0.33	2.38 (0.41–13.83)
18 mo	94	5 (5.3)	54	2 (3.7)	40	3 (7.5)	0.49	0.50 (0.07–3.64)
24 mo	82	6 (7.3)	43	0 (0)	39	6 (15.4)	—[c]	—[c]
Proximal enamel lesions on radiograph								
Baseline	242	64 (26.4)	137	38 (27.7)	105	26 (24.8)	0.45[b]	0.80 (0.45–1.44)[b]
6 mo	136	25 (18.4)	79	13 (16.5)	57	12 (21.1)	0.42	0.75 (0.38–1.49)
12 mo	115	20 (17.3)	68	12 (17.6)	47	8 (17.0)	0.79	0.90 (0.42–1.92)
18 mo	94	19 (20.2)	54	10 (18.5)	40	9 (22.5)	0.35	0.71 (0.35–1.44)
24 mo	82	14 (17.1)	43	7 (16.3)	39	7 (17.9)	0.90	0.95 (0.40–2.23)
Active white spot lesions								
Baseline	242	46 (19.0)	137	27 (19.7)	105	19 (18.1)	0.48[b]	0.77 (0.38–1.58)[b]
6 mo	136	15 (11.0)	79	8 (10.1)	57	7 (12.3)	0.71	0.85 (0.31–2.35)
12 mo	115	17 (14.8)	68	8 (11.8)	47	9 (19.1)	0.26	0.64 (0.29–1.39)
18 mo	94	8 (8.5)	54	4 (7.4)	40	4 (0.1)	0.93	1.02 (0.24–4.22)
24 mo	82	10 (12.2)	43	5 (11.6)	39	5 (12.8)	0.75	0.84 (0.30–2.36)
Restorations within prior year								
Baseline	242	188 (77.7)	137	109 (79.6)	105	79 (75.2)	0.08[b]	0.74 (0.53–1.04)[b]
6 mo	136	66 (48.5)	79	36 (45.6)	57	30 (52.6)	0.25	0.85 (0.64–1.12)
12 mo	115	26 (22.6)	68	12 (17.6)	47	14 (29.8)	0.11	0.57 (0.24–1.12)
18 mo	94	11 (11.7)	54	3 (55.6)	40	8 (20.0)	0.21	0.27 (0.04–2.11)
24 mo	82	10 (12.2)	43	5 (11.6)	39	5 (12.8)	0.70	0.73 (0.15–3.50)
Any of these 4 disease indicators								
Baseline	242	232 (95.9)	137	131 (95.6)	105	101 (96.2)	0.01[b]	0.75 (0.59–0.94)[b]
6 mo	136	90 (66.2)	79	49 (62.0)	57	41 (71.9)	0.13	0.83 (0.66–1.05)
12 mo	115	61 (53.0)	68	31 (45.6)	47	30 (63.8)	0.04	0.71 (0.51–0.98)
18 mo	94	38 (40.4)	54	17 (31.5)	40	21 (52.5)	0.04	0.61 (0.37–0.98)
24 mo	82	34 (41.5)	43	15 (34.9)	39	19 (48.7)	0.12	0.67 (0.41–1.11)

For patients classified at baseline as high caries risk, the number and percentage of patients for whom clinical disease indicators were noted during caries risk assessments are shown according to assigned treatment group.
[a]Comparing intervention to control group, adjusted for repeated measures in generalized estimating equation (GEE) models.
[b]Global contrast over all postbaseline study visits in GEE models (i.e., not time point specific).
[c]Not estimated (no events in intervention group).

participants finally recruited per each office illustrated the challenges some offices were faced with. It is of note that the offices that were successful with recruiting had integrated the CAMBRA philosophy into their daily routine and workflow. Thus, these offices easily recruited patients while other offices felt being in the study was an additional burden.

The logistical and financial challenges in tracking compliance with home use of the provided products were beyond the resource constraints of the present trial. Reliable compliance testing methods (salivary bacteria, fluoride levels) were not available.

A scenario with controls receiving only OTC toothpaste would have challenged the double-blind approach in the practice-based setting. However, it is possible that because participants in both groups were provided products without knowing whether they were part of the control or intervention, both groups were highly motivated to follow dentists' recommendations.

Conclusion

The CAMBRA-PBRN study performed by 21 dentists in private dental offices or by FQHC employees including 460 participants showed the percentage of participants assessed as high caries risk at baseline dropped constantly over the observation period of 24 mo to 25% for the intervention group applying CAMBRA preventive interventions. In contrast, the percentage of participants in the control group only dropped to 54% of participants staying at high caries risk, with the difference being statistically significant, suggesting that the provided intervention reduced caries risk level more effectively than the standard-of-care control. The majority of participants assessed at baseline as being low caries risk did not change to a higher risk level over the time, demonstrating a strong predictive value of the low caries risk classification at baseline.

Author Contributions

P. Rechmann, contributed to conception, design, and data analysis, drafted and critically revised the manuscript; B.W. Chaffee, B.M.T. Rechmann, contributed to data acquisition, analysis, and interpretation, critically revised the manuscript; J.D.B. Featherstone, contributed to conception, design, data acquisition, analysis, and interpretation, critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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