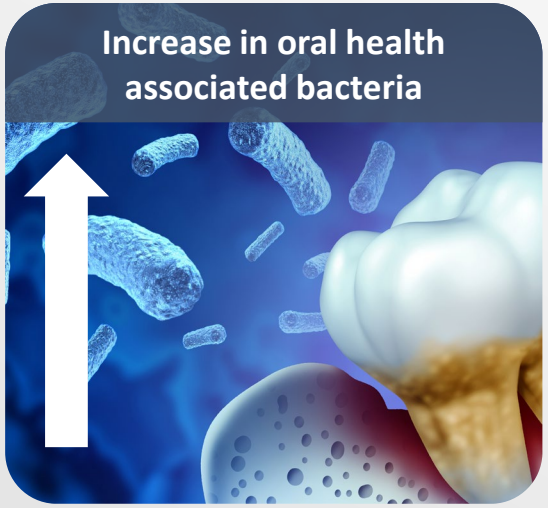
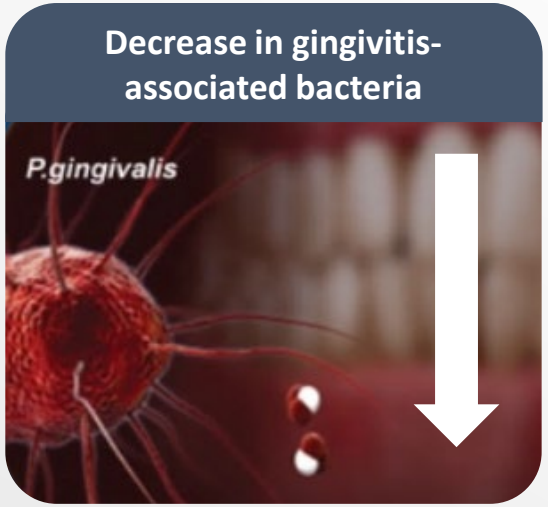
STANNOUS FLUORIDE & THE ORAL MICROBIOME:



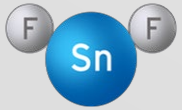


Stabilizing Effect in Natural Teeth

Short-Term Response[1] (2 Weeks)

Vs. Baseline

Long-Term Response[2] (3 Years)



Vs. Control (NaF)

[1] He et al. (2021) Am J Dent 34: 222-227
[2] Kruse et al. (2021) Antibiotics 10, 481

Stabilizing Effect Peri-Implant

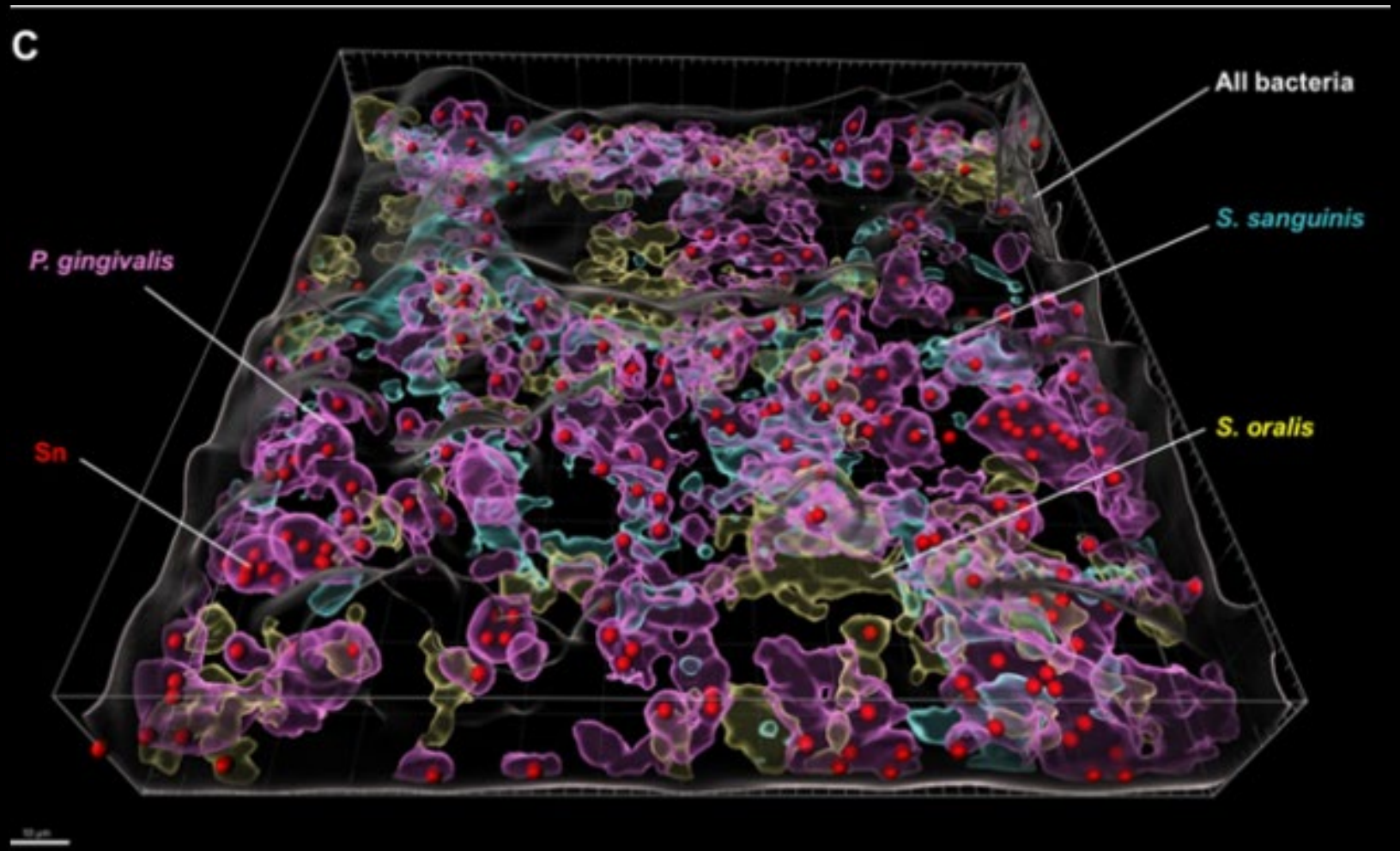
SnF_2 treatment favorably shifted oral microbiomes in peri-implant mucositis subjects toward the no-mucositis state

A 4-week SnF_2 toothpaste treatment reduced the relative abundance of Fusobacterium, Porphyromonas, Treponema, Prevotella, etc and increased the relative abundance of Rothia, Actinomyces. This change to the dental plaque microbiome composition is consistent with a return to a healthy no-mucositis microbiome and improved clinical signs and symptoms

Ramji et al. J Dent Res (Spec Iss A) 2024; 103: Abstract 2509.

Courtesy of Procter & Gamble

Sn^{2+} specific intracellular imaging reflected the colocalization of Sn^{2+} ions with *P. gingivalis* but not with other species.



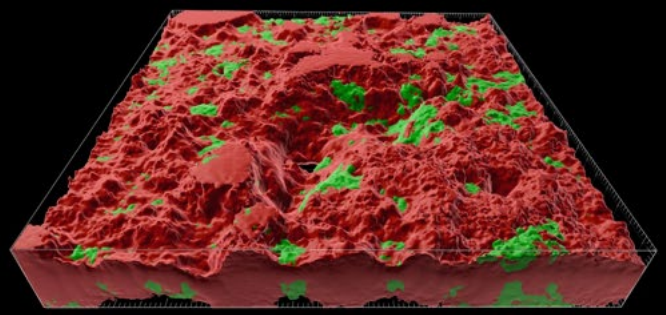
Representative FISH-CLSM and 3D reconstructed images using probes targeting specific bacterial strains and metal ions. Simultaneous hybridization for the SN treated biofilm with species-specific probes targeted for: **(C)** Combined 3D reconstructed image for SN-treated *in situ* biofilm with probes targeting for Sn^{2+} (red), *S. oralis* (yellow), *S. sanguinis* (cyan), *P. gingivalis* (purple) and non-specific white (non-specific). Bar: 10 µm.

Courtesy of Procter & Gamble

Chen, D et al. Front. Microbiol., 14 February 2024 Volume 15 - 2024 | https://doi.org/10.3389/fmicb.2024.1327913

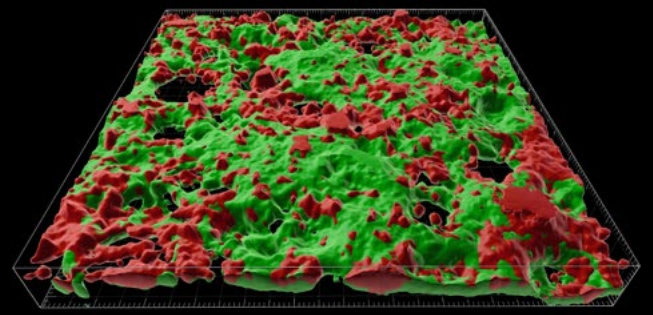
‘RED COMPLEX’ PATHOGEN VS GENERAL BACTERIA

P. GINGIVALIS, *T. FORSYTHIA*, AND *T. DENTICOLA* COMMENSAL: *S. ORALIS*,



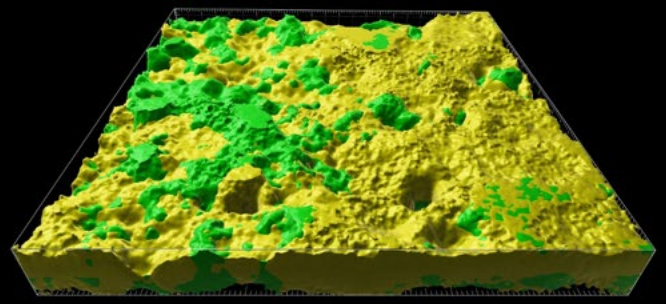
Before Stannous Fluoride

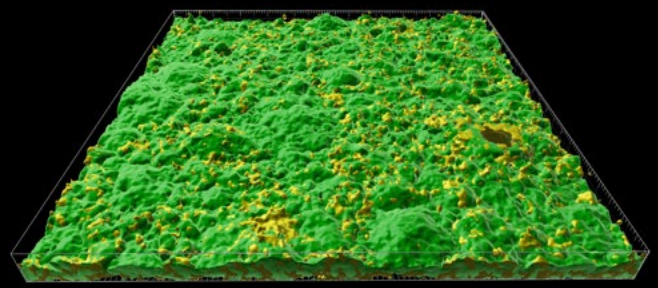
Before



After Stannous Fluoride

After





primary causative agent *S. mutans*, the pivotal “bridging species” *F. nucleatum*, and two beneficial commensals, *S. oralis* and *A. naeslundii*.

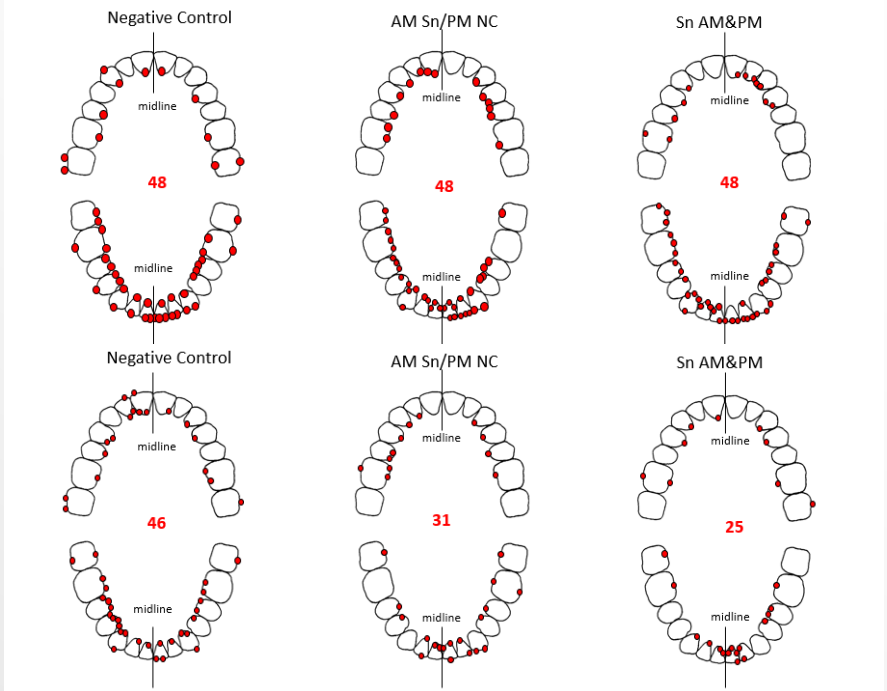
Courtesy of Procter & Gamble

Chen, D et al. Front. Microbiol., 14 February 2024 Volume 15 - 2024 | https://doi.org/10.3389/fmicb.2024.1327913

Overall Average Bleeding

Dose Dependent Response Sodium Vs Stannous

Design	3 treatment Parallel group study Randomized Controlled Trial	3 treatment Parallel group study Randomized Controlled Trial
Duration	1 month (BL, Week 4) 90 Subjects Subjects Brushed for 1 minute	12 weeks (BL, week 4, week 12) 90 subjects Subjects Brushed for 1 minute
Clinical Indices	LSGI, # of bleeding sites	LSGI, # of bleeding sites
Test Products	**3 Treatments (30/trt)** • Colgate Cavity Protection (NC, **am/pm**) • CPH Sensitive and Enamel Shield (PC, am/pm) • CPH Sensitive and Enamel Shield **am** & Colgate Cavity Protection pm (Experimental)	



Likelihood of transitioning to health:

One Time vs. None — 3X

Two times vs. One — 3.2X

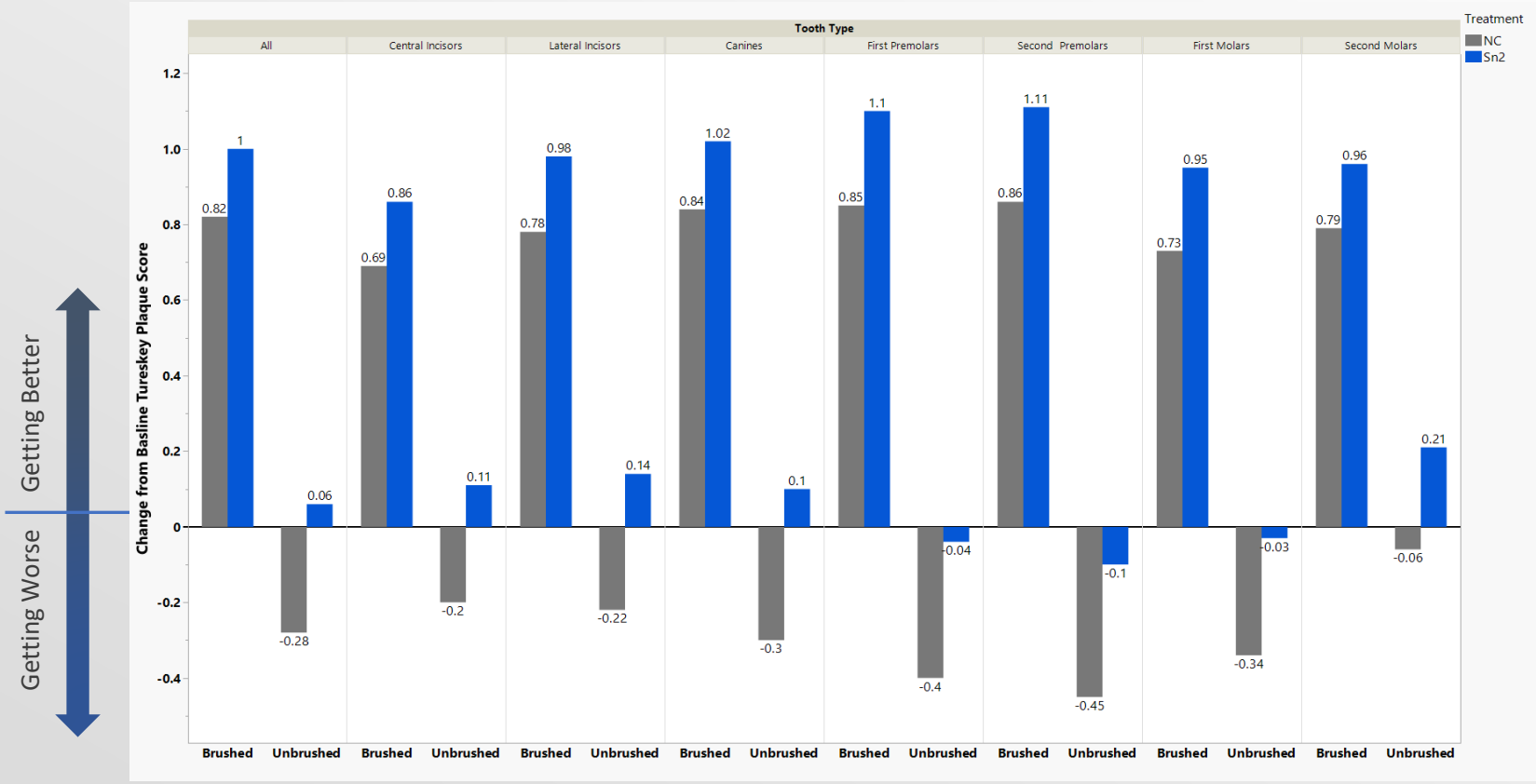
Courtesy of Procter & Gamble

Study No. 2020112

CHEMISTRY BEYOND THE BRUSH

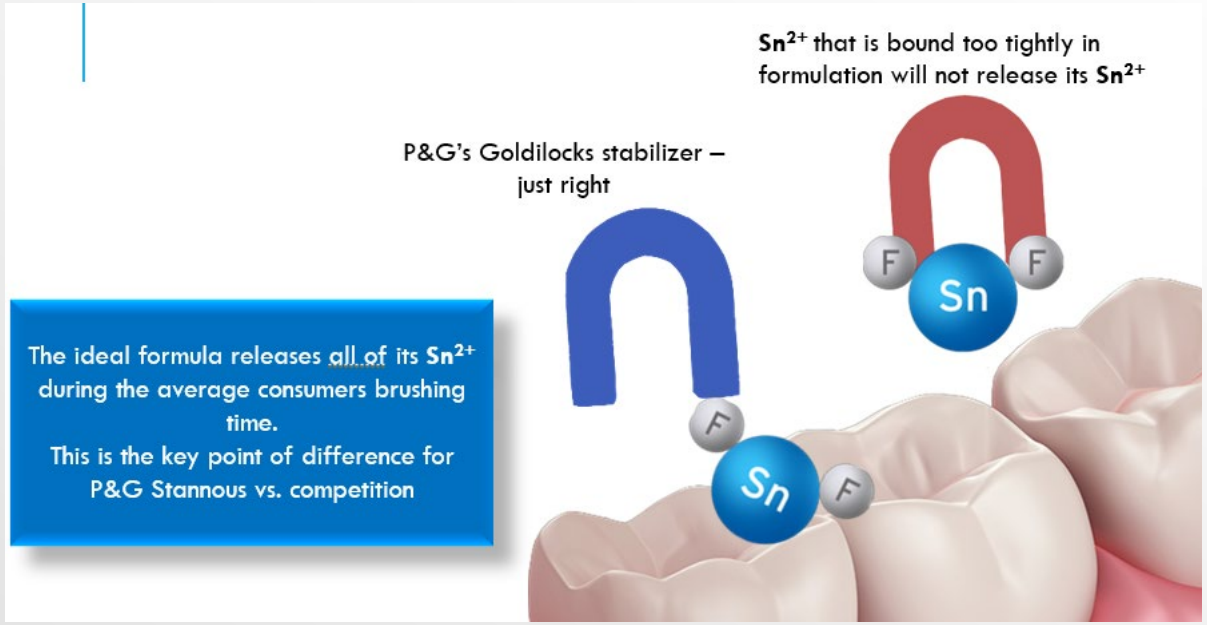
Brushed vs Unbrushed Surfaces

Plaque Score Change



Brushed = lingual surfaces; Unbrushed = buccal surfaces

Formulation Matters



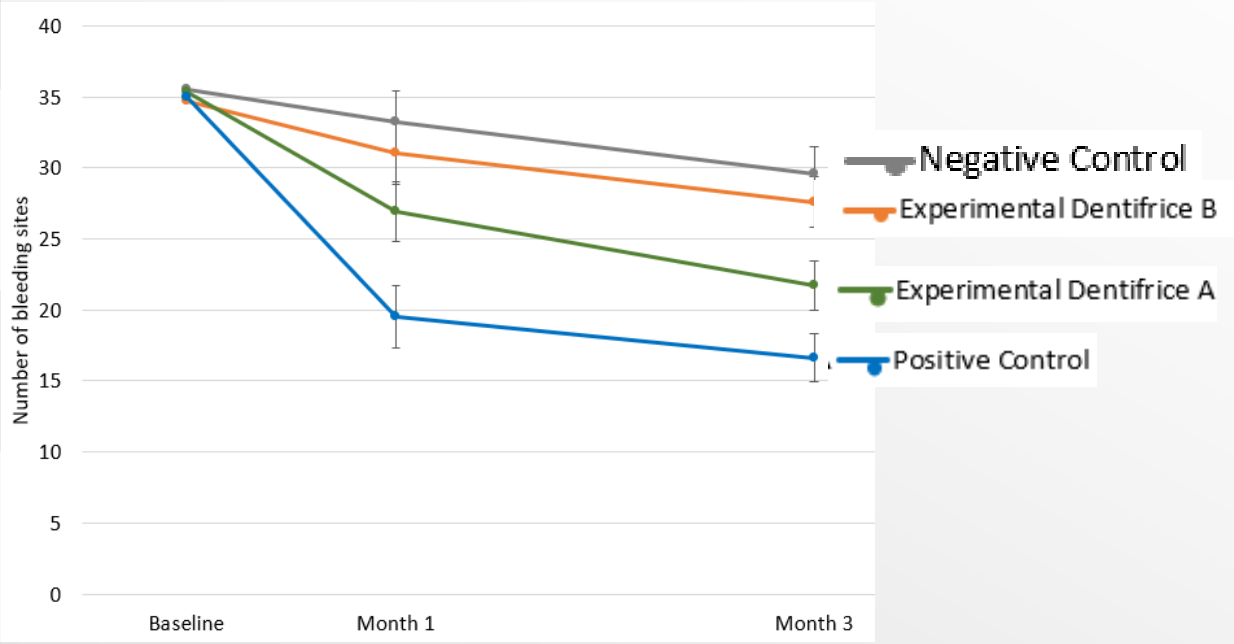
- Stannous must be in the correct oxidation state
  - Stannous in the Sn2+ is the only form shown to have gingivitis efficacy
- Stannous must be soluble
- Stannous cannot exist in nature without being bound to a negative ion (a.k.a. chelant) to make a salt
- The ideal formula has a Sn2+ salt that keeps the Sn2+ from adsorbing to the silica in toothpaste.
- Stannous must be delivered to the mouth
  - The ideal formula releases all of its Sn2+ salt during the average consumer's brushing time
  - Sn2+ that is bound too tightly in formulation will not reduce biological materials nor bind to LPS
  - Sn2+ that is not bound tightly enough in formulation will easily bind to other negative ions
- Stannous must have reductive potential in the mouth
- Stannous must release to the bacteria and the bacteria must be able to "uptake" Sn2+ in order to have the desired physiological benefits

A 3-Month Randomized Trial Evaluating Effects of Stannous Fluoride Bioavailability on Gingivitis

Objective: To assess the impact of formulation chemistry on gingivitis effects of two experimental 0.454% stannous fluoride (SnF2) dentifrices with low tin bioavailability versus positive and negative controls.

Conclusion: SnF_2 dentifrice formulation chemistry influences the level of antigingivitis efficacy, which was also reflected in tin bioavailability, tin uptake into biofilm, and bacterial glycolysis inhibition.

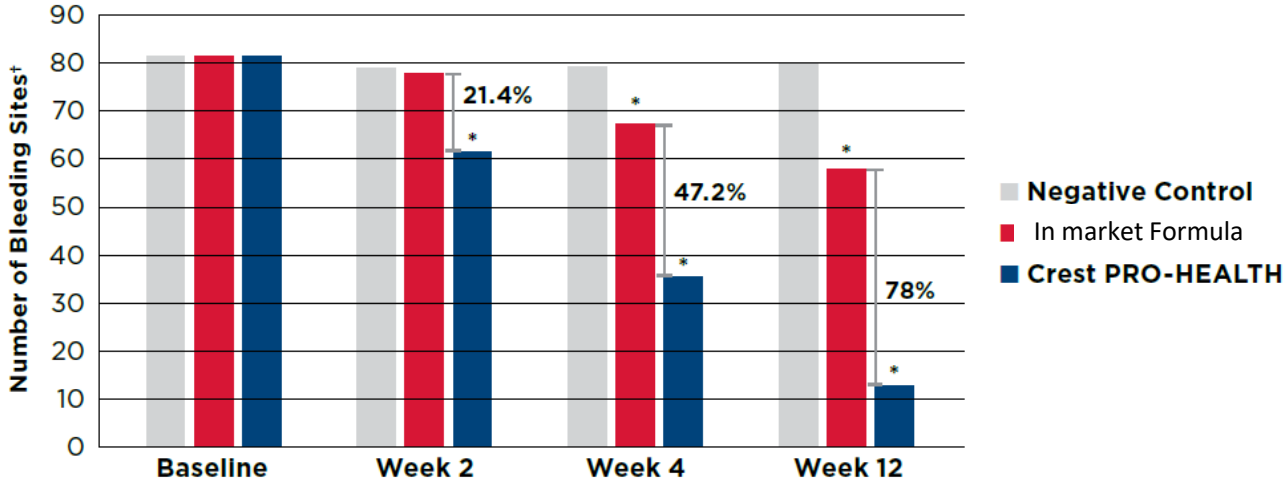
Study Design	• RCT (double blind; parallel)
Study	• 120 Participants • Measurements taken Baseline, month 1 & month 3 • Brush 1 min 2x daily • Manual toothbrush
Clinical Assessments	• Löe Silness Gingival Index (in-vivo) • Tin Uptake and Biofilm Glycolysis (In –vitro)
Legs	• Neg Ctrl : 0.76% sodium monofluorophosphate, soluble tin = 0 ppm • Experimental A: 0.454% SnF2, pH 4.7, soluble tin = 592 ppm • Experimental B: 0.454% SnF2, pH 5.8, soluble tin = 102 ppm • Positive Control: 0.454% SnF2 commercial dentifrice, soluble tin = 2037 ppm



At Months 1 and 3, the Positive Control showed significantly fewer bleeding sites versus all treatments ($p \leq 0.04$) and Experimental dentifrice A had significantly less bleeding versus the Negative Control ($p \leq 0.041$). Experimental dentifrice B was not significantly different from the Negative Control ($p \geq 0.438$) at either timepoint. Tin biofilm uptake and in vitro PGRM exhibited a similar trend.

Relative Anti-Gingivitis Efficacy of 0.454% Stannous Fluoride Dentifrices: Results from a 3-Month Randomized Controlled Trial

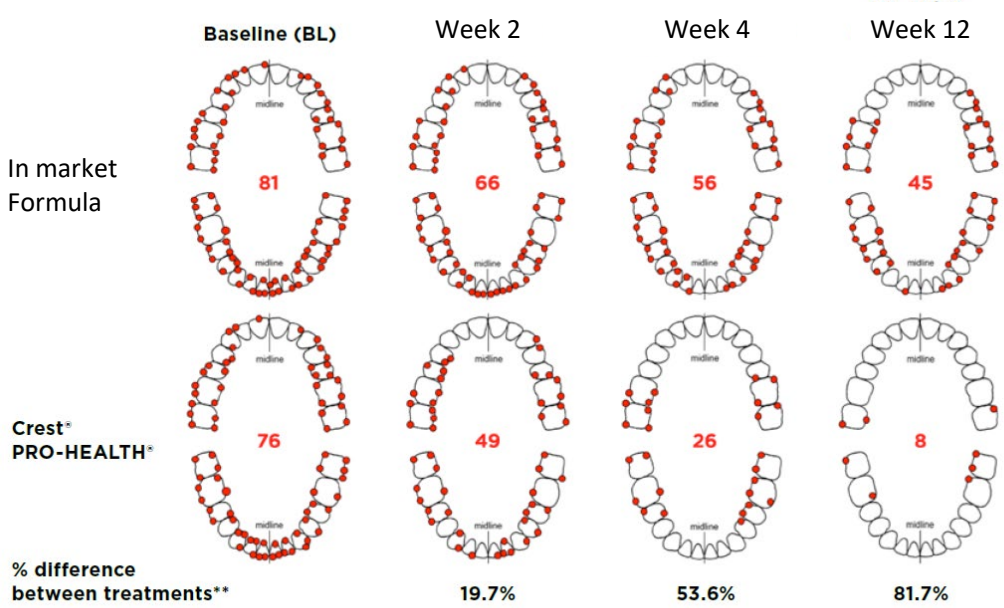
Figure 1. Number of bleeding sites per treatment group at each time point.



† Weeks 2, 4 and 12 are adjusted means. * $P<0.001$ versus negative control.

Between-group analysis showed Crest® PRO-HEALTH™ > In market Formula for bleeding site reduction at weeks 2, 4 and 12 ($P<0.001$).

Figure 2. Changes in persistent bleeding sites over time per group.



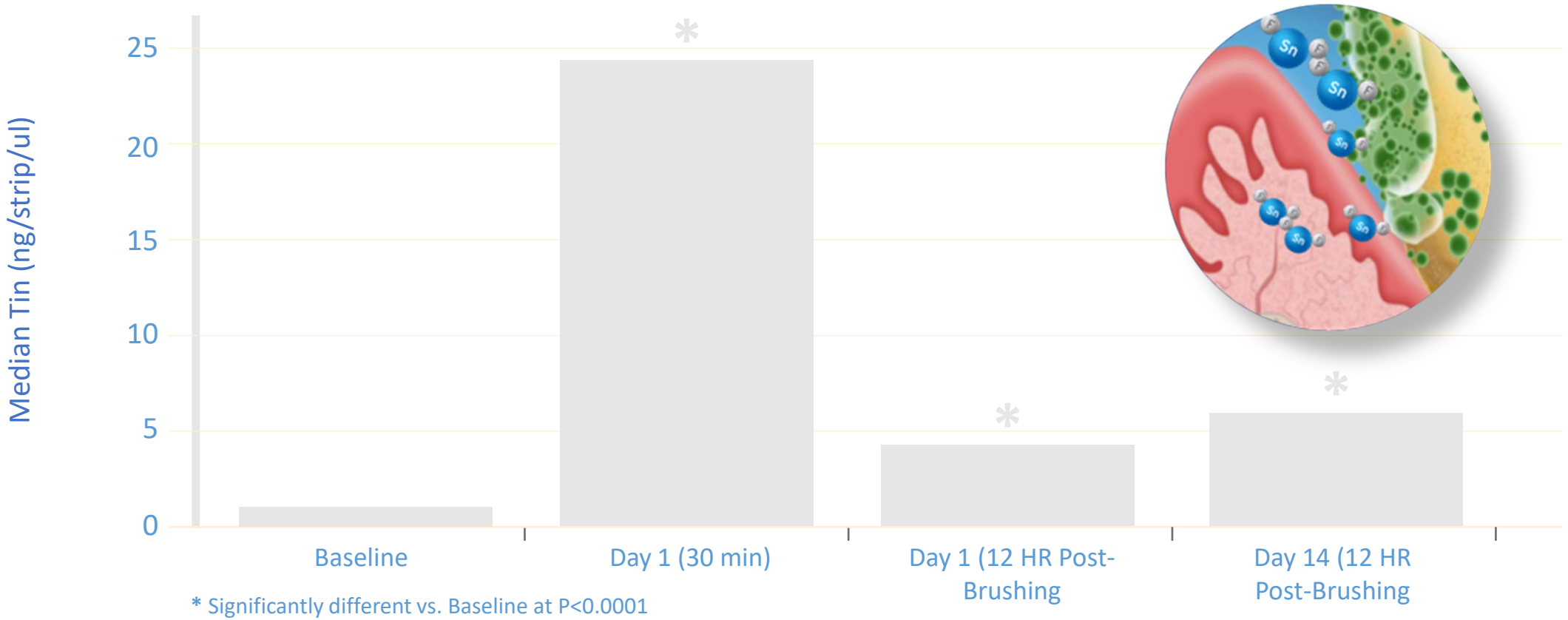
** $P<0.025$ for all timepoints

3 out of 4 subjects using Crest Stannous fluoride dentifrice moved from being classified as having generalized or localized gingivitis to generally Healthy in just 3 months vs no subject using the in-market formula

He T, Nachnani S, Lee S, Zou Y, Grender J, Farrell S, Sagel P, Biesbrock AR. The relative clinical efficacy of three 0.454% stannous fluoride dentifrices for the treatment of gingivitis over 3 months. Am J Dent. 2020 Aug;33(4):218-224. PMID: 32794398.

GINGIVITIS PROTECTION: BIOFILM PENETRATION UP TO 4MM BELOW THE GUMLINE (SUB-GINGIVAL) PENETRATION

In vivo, Stannous (tin) was detectable **up to 4mm below the gumline at 12 hours** after use of a P&G stabilized stannous fluoride formulated dentifrice



* Significantly different vs. Baseline at P<0.0001

Klukowska MA et al. Am J Dent (2018) 31: 184–188

Crest Oral-B