the Journal of CONTEMPORARY DENTAL PRACTICE at www.thejcdp.com

A Clinical Assessment of the Efficacy of a Stannous-Containing Sodium Fluoride Dentifrice on Dental Hypersensitivity

Trevor N. Day, PhD; Johannes Einwag, Prof. Dr. med. dent.; Joachim S. Hermann, PD Dr. med. dent.; Tao He, DDS, PhD; Mary Kay Anastasia, BA; Matthew Barker, PhD; Yuqing Zhang, MS

Abstract

Aim: To measure the desensitizing benefits of an experimental stannous-containing sodium fluoride dentifrice versus a regular sodium fluoride negative control.

Methods and Materials: This study was a randomized, double-blind, parallel group, four-week clinical trial. Subjects reporting dentinal hypersensitivity were enrolled and randomized to the experimental dentifrice or the control dentifrice to use twice daily for four weeks. Efficacy assessments (Air Blast) were performed at baseline and weeks two and four. Separate analyses were performed for the two most sensitive teeth at baseline and for all 12 teeth. Results for weeks two and four combined also were analyzed.

Results: Thirty-one subjects were included in the analyses. For the two most sensitive teeth, the experimental dentifrice showed statistically significantly less sensitivity ($p<0.05$) versus the control at weeks two and four and for weeks two and four combined. The sensitivity reduction ranged from 24.9% to 28.4% over the control. For all 12 teeth, the experimental group had statistically significantly ($p<0.03$) lower sensitivity scores versus the control group at week two and weeks two and four combined.

Conclusion: The experimental dentifrice demonstrated significant desensitizing advantages versus the control.

Clinical Significance: This stannous-containing sodium fluoride dentifrice provides an effective treatment for patients with dentinal hypersensitivity, significantly reducing sensitivity versus a negative control in this four-week trial.

Keywords: Stannous, dentifrice, sodium fluoride, sensitivity, clinical trial

Citation: Day TN, Einwag J, Hermann JS, He T, Anastasia MK, Barker M, Zhang Y. A Clinical Assessment of the Efficacy of a Stannous-Containing Sodium Fluoride Dentifrice on Dental Hypersensitivity. J Contemp Dent Pract [Internet]. 2010 Jan; 11(1):001-008. Available from:

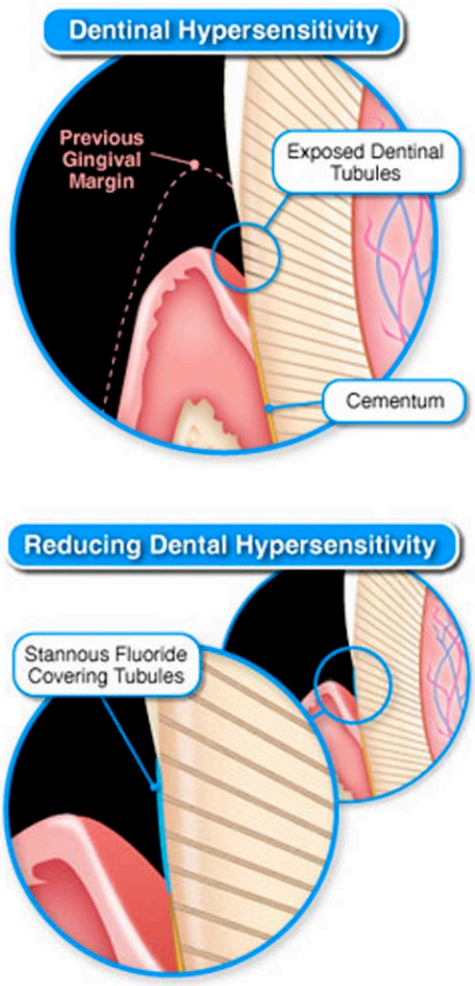
http://www.thejcdp.com/journal/view/volume11-issue1-day.

Introduction

Dentinal hypersensitivity is a highly prevalent condition reported to affect from 4% to 57% of the population.[1,2] The causes of sensitivity are well characterized as exposed dentinal tubules most commonly resulting from gingival recession followed by loss of cementum. The mechanism by which nerves are triggered to result in the pain associated with hypersensitivity is now widely accepted as that of the Brännström hydrodynamic theory.[3] This postulates that changing physical conditions on the dentin surface such as heat, pressure, or osmotic potential give rise to fluid movement in the tubules.[4–6] The consequent pressure change stimulates the nerves giving rise to the pain.

The mechanism of action of stannous ions[7] in reducing dentinal hypersensitivity has been found to be the precipitation of stannous compounds occluding the dentinal tubules and thus preventing stimulation of the nerves in the pulp cavity. *In vitro* studies using various techniques, such as scanning electron microscopy, electron probe microanalysis, and Vickers surface micro-hardness, demonstrate deposition of tin and fluoride on the surface and covering of the dentinal tubules.[8,9] One laboratory evaluation showed that while both zinc and tin covered or obturated tubules, zinc was largely removed by washing whereas tin remained covering the tubules.[10] Another study showed specimens treated with stannous fluoride (Crest® Pro-Health®, The Procter & Gamble Company, Cincinnati, OH, USA) appeared to resist acid solubilization.[9]

A number of clinical studies also have been conducted to investigate the effectiveness of stannous-containing oral care products upon dentinal hypersensitivity. Most of the early studies focused on *gels* containing 0.4% stannous fluoride,[11] whereas the majority of contemporary trials have evaluated stannous-containing *dentifrice* formulations.[12–18] The collective findings demonstrate the effectiveness of numerous stannous-containing products in reducing sensitivity.



Recently, a new stannous-containing sodium fluoride dentifrice was developed. This clinical trial was conducted to evaluate the effectiveness of this formulation relative to a negative control for the treatment of dentinal hypersensitivity.

Methods and Materials

Study Design

This was a randomized, parallel group, double-blind, four-week clinical trial to assess changes in subject perceived tooth hypersensitivity via air blast induced examiner grade assessment among subjects using a stannous-containing sodium fluoride dentifrice compared to those using a negative control dentifrice. Measurements were conducted at baseline, week two, and week four visits.

Entrance Criteria

Following Ethics Committee approval, at least 30 generally healthy adults age 18–70 reporting tooth sensitivity were sought. Subjects had to agree to refrain from using anti-hypersensitivity products or having elective dental procedures (including prophylaxis) performed during the study.

Subjects who were currently using an anti-sensitivity toothpaste or another anti- sensitivity product or who had used such a product in the previous month were excluded. Subjects with carious teeth or with any other condition that the investigator considered may compromise the results also were excluded. Subjects taking daily doses of anticonvulsants, sedatives, tranquilizers, or other mood-altering drugs were excluded as well as subjects with a history of significant adverse effects following the use of oral hygiene products such as toothpaste and mouth rinse.

Test Dentifrices, Assignment to Treatment Sequence

The two treatments used in this study were

1. An experimental stannous-containing sodium fluoride dentifrice with 1450 ppm F- sodium fluoride and stannous chloride as a key excipient (Procter & Gamble UK, Surrey, United Kingdom)
2. Crest® Decay Protection (UK) with 1450 ppm F- sodium fluoride (Procter & Gamble UK, Surrey, United Kingdom)

Both were supplied to the subjects with (medium) Oral-B Advantage 40 toothbrushes (The Procter & Gamble Company, Cincinnati, OH, USA). The test products were supplied in kits containing the assigned toothpaste, toothbrush, and written usage instructions. The dentifrice in both kits was supplied blinded in white tubes.

Subjects were stratified at baseline into one of four strata depending on their gender (female or male) and the baseline self-reported tooth hypersensitivity (low or high). Within strata, subjects were randomly assigned to one of the two treatment groups using an encoded program. Subjects residing in the same household were assigned to the same treatment group.

Treatment Regimens

Subjects used the assigned products for the first time under supervision at the clinical site. Subjects used the products at home in place of their normal toothbrush and dentifrice for a period of four weeks. Subjects were instructed to brush twice daily for two minutes each time. Subjects were instructed not to alter their other oral hygiene habits (e.g., flossing) with the exception that no anti–tooth hypersensitivity products should be used.

Air Blast Tooth Specific Sensitivity Assessment

The thermal sensitivity perceived by the subject was measured by the examiner by directing an air blast individually at each of the premolars and canines at baseline, week two, and week four visits. Each tooth was isolated with cotton rolls and the air blast was delivered from a distance of 1.0 centimeter for 1 second. The following scale[19] was used by the examiner to assess the level of

hypersensitivity for each of the 12 teeth examined:

- 0 – Absence of pain, but perceiving stimulus
- 1 – Slight pain
- 2 – Pain during application of stimulus
- 3 – Pain during application of stimulus and immediately thereafter

Statistical Methods

For air blast–induced hypersensitivity scores, separate analyses were performed for the two teeth with the most sensitivity at baseline and for all 12 teeth combined. Analysis of covariance (ANCOVA) with treatment as a factor and the baseline score and age as the covariates were used to assess treatment differences in hypersensitivity at the post-baseline visits. Also for the hypersensitivity scores, separate repeated measures models were used to investigate the overall relationship between the treatment groups and the post-baseline visits (weeks two and four) with statistical testing for the interaction and overall treatment effects using a two-sided 5% significance level. In this study, the interaction between treatment and week was not statistically significant ($p>0.45$) for each hypersensitivity score, and the interaction was removed from the repeated measures model.

Results

Thirty-one subjects were enrolled at the baseline visit, received product, and completed the study through week four. Subjects ranged in age from 23 to 65 years with an average of 42 years, and 68% of the subjects were female. The treatment groups were balanced ($p>0.86$) for all demographic characteristics. Mean baseline scores were not significantly different ($p>0.56$) between groups at baseline for either the two most sensitive teeth or for all 12 teeth combined.

Efficacy Results

At the week two and week four post-baseline visits and combining weeks two and four, the experimental group had mean air blast scores for two most sensitive teeth that were 28.4%, 24.9%, and 27% lower, respectively, than the control group ($p<0.05$, Figure 1). At week two, mean scores for the experimental and control groups were 1.51 and 2.11, respectively (Table 1). At week four, the experimental group had a mean score of 1.42 compared to 1.89 for the control group. The weeks two and four combined mean score was 1.46 for the experimental group and 2.00 for the control group.

Table 1. Between treatment comparison of air blast score for two most sensitive teeth.

Visit/Treatment	N	Mean (SE)[a]	Two-Sided *p*-Values
Baseline			
Experimental Sn Dentifrice	15	2.17 (0.105)	0.5605
Crest Decay Prevention	16	2.31 (0.218)	
Week two			
Experimental Sn Dentifrice	15	1.51 (0.153)	0.0089
Crest Decay Prevention	16	2.11 (0.148)	
Week four			
Experimental Sn Dentifrice	15	1.42 (0.158)	0.0416
Crest Decay Prevention	16	1.89 (0.153)	
Week two and four[b]			
Experimental Sn Dentifrice	15	1.46 (0.128)	0.0053
Crest Decay Prevention	16	2.00 (0.124)	

[a] Week two and four means adjusted for the baseline value and age.
[b] Overall results pooling weeks two and four from the repeated measures analysis.

Table 2. Between treatment comparison of air blast score for all 12 teeth.

Visit/Treatment	N	Mean (SE)[a]	Two-Sided *p*-Values
Baseline			
Experimental Sn Dentifrice	15	1.34 (0.137)	0.9893
Crest Decay Prevention	16	1.34 (0.141)	
Week two			
Experimental Sn Dentifrice	15	1.18 (0.098)	0.0196
Crest Decay Prevention	16	1.52 (0.095)	
Week four			
Experimental Sn Dentifrice	15	1.16 (0.095)	0.0748
Crest Decay Prevention	16	1.40 (0.092)	
Week two and four[b]			
Experimental Sn Dentifrice	15	1.17 (0.084)	0.0213
Crest Decay Prevention	16	1.46 (0.082)	

[a] Week two and four means adjusted for the baseline value and age.
[b] Overall results pooling weeks two and four from the repeated measures analysis.

At week two and combining weeks two and four, the experimental group provided significantly ($p<0.03$) lower mean air blast scores for all 12 teeth relative to the control group (Table 2).

The experimental group had a mean score of 1.18 at week two while the mean score for the control group was 1.52. The weeks two and four combined score was 1.17 for the experimental group and 1.46 for the control. At the week four visit, the experimental group provided directionally ($p=0.07$) lower mean air blast scores for all 12 teeth relative to the control group (1.16 and 1.40, respectively). This difference was not statistically significant using a two-sided 5% significance level. The desensitizing benefit of the experimental dentifrice over the control was 22.4% at week two, 17.1% at week four, and 19.9% for the combined weeks two and four visits (Figure 1).

Safety Results

One subject in the experimental group had a possible related adverse event (desquamation) observed by the examiner that was mild in nature. Another subject in the experimental group had a nontreatment-related adverse event (herpetic lesion) reported and observed that was mild in nature.

Discussion

In this clinical trial, the experimental group exhibited a significantly greater reduction in tooth sensitivity via air blast measurements than the control among the two most sensitive teeth ($p<0.05$) at both post-baseline measurements and the combined weeks two and four visits. The experimental group also demonstrated significantly greater reductions than the control in tooth sensitivity via air blast measurements among all 12 teeth on post-baseline measurements at week two and the combined results for weeks two and four ($p<0.03$). The assessment of all 12 teeth was included in this trial for comparative purposes but is not a widely used measure in sensitivity trials since the condition typically does not affect each tooth.

These results are aligned with other studies evaluating stannous-containing dentifrices. Five trials in the literature evaluated the desensitizing effects of a combination of 0.454% stannous fluoride and 5% potassium nitrate relative to other products; four trials compared the dentifrice to a positive control sensitivity toothpaste containing 5% potassium nitrate and the fifth study was versus a commercial nondesensitizing control dentifrice.[12–16] The effectiveness of the product

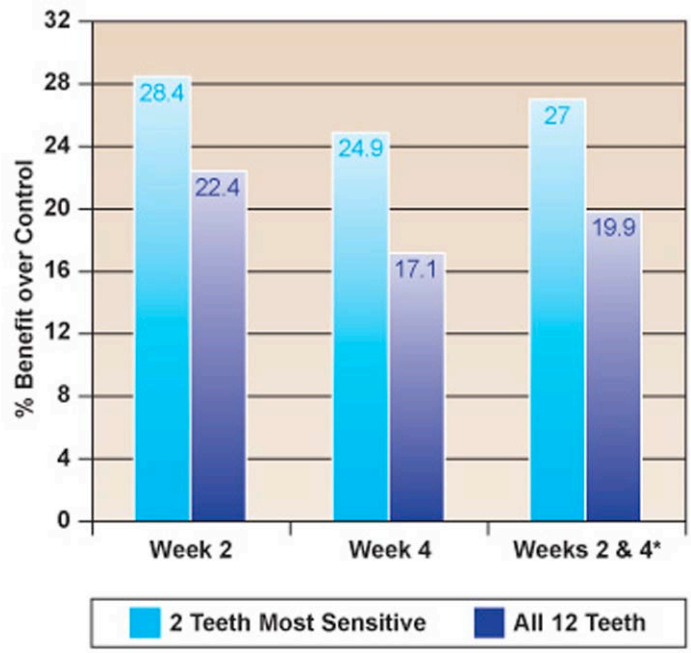


Figure 1. Overall results pooling weeks two and four from the repeated measures analysis.

containing the combination of stannous fluoride with potassium nitrate was found to be greater than that of the sodium fluoride product with potassium nitrate[12–15] and the nondesensitizing control.[16] Two published randomized parallel group studies were conducted on a dentifrice containing stannous fluoride compared to a sodium fluoride negative control toothpaste.[17,18] In both studies, the sensitivity scores of the stannous fluoride group after four and eight weeks of product usage were statistically significantly lower than the control toothpaste group, demonstrating the effectiveness of the stannous fluoride toothpaste in reducing dentinal hypersensitivity.

In addition, the significant reductions in dentinal hypersensitivity demonstrated by the stannous-containing sodium fluoride dentifrice, now marketed in parts of Europe and China, are consistent with outcomes of other research on this particular formulation. An eight-week, randomized, parallel group, two treatment, double-blind study was conducted among generally healthy adults with moderate thermal and tactile dentinal hypersensitivity.[20] Subjects were stratified at baseline according to age, gender, and thermal dentinal sensitivity scores and randomly assigned to one of the two treatments: the new stannous-containing sodium fluoride dentifrice or a marketed potassium nitrate control (Crest® Sensitivity Protection, The Procter & Gamble Company, Cincinnati, OH, USA) for twice daily usage. Hypersensitivity was assessed via Yeaple Probe and cold Air Blast/Schiff Air Index for tactile and thermal assessments respectively, at baseline, week four, and week eight. Fifty-eight subjects completed all evaluations. Both treatments produced significant ($p<0.05$) reductions in hypersensitivity compared to baseline at both week four and week eight time points. There

were no significant differences between the two treatments at either week four or week eight ($p>0.534$) for either assessment.

One advantage of this stannous-containing sodium fluoride dentifrice formulation relative to other desensitizing treatments is its effectiveness against other common oral conditions. A recent study by He and colleagues evaluated its plaque prevention efficacy relative to a positive (Colgate®Total®, Colgate-Palmolive, New York, NY, USA) and negative (Crest® Cavity Protection, The Procter & Gamble Company, Cincinnati, OH, USA) control dentifrice.[21] Following a dental polish, subjects brushed lingual surfaces only, then swished with a slurry of the dentifrice over the entire dentition twice per day over a four-day period. At baseline and after four days, plaque levels were assessed by the Turesky Modification of the Quigley–Hein plaque index (TMQHPI). The whole mouth TMQHPI plaque scores after treatment for both the experimental and the positive control dentifrices were statistically significantly lower than those for the negative control by 11.4% and 8.4%, respectively ($p<0.0001$).

Another recent study showed the benefit of this stannous-containing sodium fluoride dentifrice against extrinsic stain.[22] While many stannous fluoride products can produce minor extrinsic tooth stain, this formulation uses a polychelation technology to stabilize the stannous-fluoride complex and prevent stain. The study also included an experimental stannous-containing dentifrice, a nonstaining marketed dentifrice (Colgate® Total®), and a stannous fluoride dentifrice (Crest® Gum Care, The Procter & Gamble Company, Cincinnati, OH, USA) previously established to induce extrinsic stain. Following a baseline Lobene stain examination, subjects received a prophylaxis on the 12 anterior teeth to remove extrinsic stain and tartar. Subjects were randomly assigned based on baseline stain scores to receive one of the four treatments and to use them twice daily over a five-week period. Results showed that there was significantly less stain after product use in the new stannous-containing sodium fluoride dentifrice group, the experimental stannous-containing sodium fluoride dentifrice group, and the Colgate Total group compared to the Crest Gum Care group ($p<0.0001$). There were no other statistically significant treatment differences between the two stannous-containing sodium fluoride groups and the Colgate Total group at either time point for any Lobene measures ($p>0.145$).

Further research is warranted on this formulation to demonstrate the full breadth, as well as magnitude, of benefits.

Conclusion

The stannous-containing sodium fluoride dentifrice provides statistically significant benefits for dentinal hypersensitivity and should be considered as a home care option for patients who experience this condition.

Clinical Significance

This stannous-containing sodium fluoride dentifrice provides an effective treatment for patients with dentinal hypersensitivity.

References

1. Rees JS, Addy M. A cross-sectional study of buccal cervical sensitivity in UK general dental practice and a summary review of prevalence studies. Int J Dent Hyg. 2004; 2(2):64-9.
2. Irwin CR, McCusker P. Prevalence of dentine hypersensitivity in a general dental population. J Ir Dent Assoc. 1997; 43(1):7-9.
3. Jacobsen PL, Bruce G. Clinical dentin hypersensitivity: understanding the causes and prescribing a treatment. J Contemp Dent Pract. 2001; 2(1):1-12.
4. Rosenthal MW. Historic review of the management of tooth hypersensitivity. Dent Clin North Am. 1990; 34(3):403-27.
5. Brännström M, Aström A. The hydrodynamics of the dentine; its possible relationship to dentinal pain. Int Dent J. 1972; 22(2):219-27.
6. Kramer IRH. The relationship between dentine sensitivity and movements in the contents of the dentinal tubules. Br Dent J. 1955; 98: 391-2.
7. Miller S, Truong T, Heu R, Stranick M, Bouchard D, Gaffar A. Recent advances in stannous fluoride technology: antibacterial efficacy and mechanism of action towards hypersensitivity. Int Dent J. 1994; 44(1 Suppl 1):83-98.

8. Ellingsen JE, Rölla G. Treatment of dentin with stannous fluoride—SEM and electron microprobe study. Scand J Dent Res. 1987; 95(4):281-6.
9. White DJ, Lawless MA, Fatade A, Baig A, von Koppenfels R, Duschner H, Götz H. Stannous fluoride/sodium hexametaphosphate dentifrice increases dentin resistance to tubule exposure in vitro. J Clin Dent. 2007; 18(2):55-9.
10. Addy M, Mostafa P. Dentine hypersensitivity. I. Effects produced by the uptake *in vitro* of metal ions, fluoride and formaldehyde onto dentine. J Oral Rehabil. 1988; 15(6):575-85.
11. Thrash WJ, Dodds MW, Jones DL. The effect of stannous fluoride on dentinal hypersensitivity. Int Dent J. 1994; 44(1 Suppl 1):107-18.
12. Schiff T, Bonta Y, Proskin HM, DeVizio W, Petrone M, Volpe AR. Desensitizing efficacy of a new dentifrice containing 5.0% potassium nitrate and 0.454% stannous fluoride. Am J Dent. 2000; 13(3):111-5.
13. Sowinski JA, Bonta Y, Battista GW, Petrone D, DeVizio W, Petrone M, Proskin HM. Desensitizing efficacy of Colgate Sensitive Maximum Strength and Fresh Mint Sensodyne dentifrices. Am J Dent. 2000; 13(3):116-20.
14. Sowinski JA, Battista GW, Petrone ME, Chaknis P, Zhang YP, DeVizio W, Volpe AR, Proskin HM. A new desensitizing dentifrice—an 8-week clinical investigation. Compend Contin Educ Dent Suppl. 2000; (27):11-6.
15. Schiff T, Zhang YP, DeVizio W, Stewart B, Chaknis P, Petrone ME, Volpe AR, Proskin HM. A randomized clinical trial of the desensitizing efficacy of three dentifrices. Compend Contin Educ Dent Suppl. 2000; (27):4-10.
16. Conforti N, Battista GW, Petrone DM, Petrone ME, Chaknis P, Zhang YP, DeVizio W, Volpe AR, Proskin HM. Comparative investigation of the desensitizing efficacy of a new dentifrice: a 14-day clinical study. Compend Contin Educ Dent Suppl. 2000; (27):17-22.
17. Schiff T, He T, Sagel L, Baker R. Efficacy and safety of a novel stabilized stannous fluoride and sodium hexametaphosphate dentifrice for dentinal hypersensitivity. J Contemp Dent Pract. 2006; 7(2):1-8.
18. Schiff T, Saletta L, Baker RA, Winston JL, He T. Desensitizing effect of a stabilized stannous fluoride/Sodium hexametaphosphate dentifrice. Compend Contin Educ Dent. 2005; 26(9 Suppl 1):35-40.
19. Giniger M, Macdonald J, Ziemba S, Felix H. The clinical performance of professionally dispensed bleaching gel with added amorphous calcium phosphate. J Am Dent Assoc. 2005; 136(3):383-92. Comment in: J Am Dent Assoc. 2005; 136(9):1214, 1216; author reply 1216, 1218.
20. Ni L, He T, Chang A, Sun L. The desensitizing efficacy of a novel stannous-containing sodium fluoride dentifrice: an 8-week randomized and controlled clinical trial. Am J Dent. Accepted for publication in 2010.
21. He T, Sun L, Li S, Ji N. The anti-plaque efficacy of a novel stannous-containing sodium fluoride dentifrice: a randomized and controlled clinical trial. Am J Dent. Accepted for publication in 2010.
22. He T, Dunavent, JM, Fiedler SK, Baker RA. A randomized clinical study to assess the extrinsic staining profiles of stannous- and triclosan-containing dentifrices. Am J Dent. Accepted for publication in 2010.

About the Authors

Trevor Day, PhD (Corresponding Author)

Dr. Day is a Senior Clinical Scientist at the London Innovation Centre of the Procter & Gamble Company in Egham, Surrey, UK. He received his PhD in Chemistry from the University of Southampton, UK, in 1994. Since then he has held a number of positions in P&G Oral Care Research and Development and has been responsible for clinical testing in Europe for the last four years. Since holding this position he has presented at a number of major dental meetings.

e-mail: day.tn@pg.com

Johannes Einwag, Prof. Dr. med. dent.

Dr. Einwag is Professor and head of the Institute of Continuing Dental Education in Stuttgart, Germany. He graduated from the School of Dentistry in Bonn (former capital of the Federal Republic of Germany) and received his professorship at the University of Würzburg. His current research interests are

focussed on clinical studies in cariology (especially fluorides and toxicology of fluoride) and periodontology. His overall interest is to shorten the transfer period from basic scientific knowledge to daily clinical practice. He is president of the Society for Preventive Dentistry in Germany.

Joachim S. Hermann, PD Dr. med. dent.

Dr. Hermann holds a number of associate professorships at dental schools in Germany, Switzerland, and the USA. Currently, he is practicing in Zurich, Switzerland, and, in addition, is chairing an International Continuing Education Academy at the same location. He graduated from the University of Tübingen and received his PD from University of Basel. His principal research interests are implantology and periodontics and he is the author of numerous publications in these fields.

Tao He, DDS, PhD

Dr. Tao He is a Senior Clinical Scientist in Global Oral Care Clinical, Procter & Gamble Company (Cincinnati, Ohio). She received a DDS degree from Capital University of Medicine (Beijing) and a PhD degree in periodontology from Tokyo Medical & Dental University. Her current research interests include periodontal therapy, design of clinical trials, and global clinical research. Dr. He has published her research extensively, including over 60 peer-reviewed publications (manuscripts and abstracts).

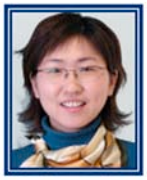
Mary Kay Anastasia, BA

Ms. Anastasia is a Principal Researcher in statistics supporting the Global Oral Care Clinical Department of the Procter & Gamble Company in Mason, OH, USA. She received her degree in mathematics at Thomas More College in 1992 before joining P&G. She has supported Oral Care for most of the last 17 years. Her research interests include clinical study design and analysis, oral care whitening, and digital image analysis. She has published several peer-reviewed manuscripts and abstracts in this area.

Matthew Barker, PhD

After receiving his PhD in statistics from the University of Kentucky, Dr. Barker joined the Procter & Gamble Company as a Statistician supporting the Global Oral Care Clinical department located in Mason, OH, USA. Dr. Barker is currently a Senior Statistician responsible for designing, sizing, analyzing, and reporting results, and he has performed these duties for over 100 clinical studies evaluating the safety and efficacy of oral care products. Dr. Barker has published his research extensively, including more than 100 peer-reviewed publications (manuscripts and abstracts).

Yuqing Zhang, MS



Ms. Zhang is a Principal Researcher in Oral Care Clinical, Proctor & Gamble (Beijing) Technology Co., Ltd. in China, where she has worked since 2000. She received a bachelor's degree in nursing from Peking Union Medical College and a master's degree in health science from University of Sydney. As a clinical trial manager based in Beijing, Ms. Zhang was responsible for clinical trial operation in more than 50 clinical trials both regionally and globally.