The Journal of Clinical Dentistry®

THE INTERNATIONAL JOURNAL OF ORAL CARE PRODUCT RESEARCH

www.JClinDent.com

Volume XXVIII **2017** **Number 1 Special Issue A**

The Journal of Clinical Dentistry (ISSN 0895-8831) is published by Professional Audience Communications, Inc., P.O. Box 39486, Charlotte, NC 28278. POSTMASTER; Send address change to P.O. Box 39486, Charlotte, NC 28278.

The Journal of *Clinical Dentistry* has been accepted for inclusion on MEDLINE, the BIOSIS, SCISEARCH, BIOMED and EMBASE databases, and the Automatic Subject Citation Alert.

Philips Sonicare and Evidence-based Innovation: Closing the Gap Between Clinical Research and Dental Practice

Maha Yakob, PhD, RDH

Global Director, Professional Relations & Scientific Affairs
Philips Oral Healthcare

In the 25 years since the widespread availability of powered products in the home oral care space, much has been learned about the complexity with which oral health is achieved and maintained. We now know that inherited factors play a role and that the inflammatory condition of periodontitis can be associated with systemic comorbidities of various types. We know that lifestyle choices play an important role and that host-defense strategies are highly influential across the health-disease spectrum. Underlying this growth in scientific understanding, we continue to explore, with the scientific fascination that compels discovery of all types, that dental plaque is much, much more than it seems. This filmy layer that is in a state of perpetual growth and renewal is a complex biofilm. It interacts in a dynamic milieu where bacterial constituents, their byproducts, cytokines, and biomarkers are in constant flux, both above and below the gingival margin.

It is noted, however, that in spite of this burgeoning advancement in our collective understanding of oral health and disease, one principle about achieving and maintaining oral health has changed very little. Daily plaque control is essential to oral health. The important difference now, however, is that we have more insight into *why* this is so. Put simply, daily plaque control helps limit the proliferation of bacterial species, their byproducts, and corresponding host signals to create an inflammatory state that exhibits itself, initially, as gingival inflammation, and when left untreated, as periodontitis.

As an innovator in the space of home oral hygiene, Philips takes daily plaque control very seriously. We know that a patient's lifestyle choices influence oral status in the short and long term. These choices, such as smoking, can favor a disease-associated environment, or they can also promote a health-associated environment. A daily tooth brushing encounter or interdental cleaning session is an opportunity to promote health, so why not make the most of it? Our aim is to constantly innovate with this top of mind; to evaluate where dental, physical, materials, mechanical, design, and behavioral sciences can be utilized to make better home oral care products to help your patients make the most of their morning and evening oral hygiene habits.

As with any medical recommendation that is intended to elicit a change in a patient's health, a specific prescription ought to have its basis in evidence that demonstrates the desired efficacy and safety effects. Within this Special Issue of *The Journal of Clinical Dentistry*® are five articles reporting the outcomes of controlled clinical trials designed to evaluate the clinical efficacy and safety of Philips home oral hygiene products, thus to provide this basis of evidence. These studies were designed, conducted, and analyzed with the statistical rigor and ethical attributes of clinical trial conduct, consistent with the regulatory statutes purported by global agencies and governing bodies that regulate the development of medical devices, drugs, and biologics. We do not take lightly a professional recommendation that can affect a patient's oral health status. Thus, it is our implicit way of working to hold ourselves to a standard that you can expect will deliver on helping your patients achieve and maintain oral health.

Contents

The Effect of Use of a Sonic Power Toothbrush and a Manual Toothbrush Control on Plaque and Gingivitis

Marcia Delaurenti, RDH, MS Marilyn Ward, DDS Sonia Souza, PhD Wendy Jenkins, BA

Philips Healthcare
Bothell, WA, USA

Mark S. Putt, PhD, MSD

University Park Research Center
Ft. Wayne, IN, USA

Kimberly R. Milleman, RDH, BSEd, MS Jeffery L. Milleman, DDS, MPA

Salus Research
Ft. Wayne IN, USA

Abstract

- **Objective:** To compare the ability of the Philips Sonicare DiamondClean power toothbrush and the ADA Reference manual toothbrush to reduce plaque and gingival inflammation by routine manual toothbrush users.
- **Methods:** This was a randomized, single-blind, parallel-design study. Eligible subjects were generally healthy non-smokers who exhibited mild to moderate gingivitis upon study entry. Enrolled subjects were randomly allocated to commence twice-daily home use of either a Philips Sonicare DiamondClean (DiamondClean) power toothbrush or an ADA reference manual toothbrush (MTB) for a period of four weeks. Clinical safety and efficacy were assessed after a two- and four-week period of home use. Statistical analysis was performed for the modified intent to treat (mITT) population using a mixed model with the Baseline score as a covariate.
- **Results:** A total of 182 volunteers were screened, 144 (72 per treatment) were randomized, and 142 subjects completed this study. Following four weeks of use, the Least Square (LS) Mean (SE) percent reduction in surface plaque was 34.9% (1.8) for DiamondClean and 8.0% (1.7) for MTB, ($p < 0.0001$). At the same four-week time point, the LS Mean (SE) percent reduction in gingival inflammation for DiamondClean was 25.5% (1.9) and 19.1% (1.9) for MTB ($p = 0.0213$). For gingival bleeding, the LS Mean (SE) percent reduction in sites with gingival bleeding for DiamondClean was 57.4% (3.06) and 31.4% (3.04) for MTB ($p < 0.0001$).
- **Conclusion:** The Philips Sonicare DiamondClean power toothbrush was statistically significantly more effective than a manual toothbrush in reducing supragingival plaque, gingival inflammation, and gingival bleeding following a four-week period of home use. Both products were safe for home use.

(J Clin Dent 2017;28(Spec Iss A):A1–6)

Introduction

Dental plaque is a dynamic biofilm that harbors an ecologically diverse array of microbes.[1,2] Its constituent ecology and impact on oral health is affected by many factors. Inherited genetics, environmental factors, lifestyle choices, and other diseases are among the elements that can affect its mosaic and elastic composition.[3,4] Innovations in measurement techniques have enabled the scientific community to characterize the species of microbes that comprise the seemingly amorphous film of plaque that coats tooth surfaces and the adjacent sulcular spaces.[5,6]

There are microbes that are generally associated with health and those that signify disease;[7] there are microbial communities that reflect lifestyle choices[8-10] (*e.g.*, smoking), and these communities of microbes communicate with other species in the plaque milieu.[11] Their constituent presence can affect responses in the host that can have both local effects, evident as periodontal disease, and potentially systemic effects.[12-17] Thus, the seemingly simple habit of daily mechanical plaque removal has a potentially far reaching impact, and efforts to help patients improve daily oral care are warranted.

The Philips Sonicare power toothbrush (Bothell, WA, USA) was developed for this purpose. It is one of several tools that patients can adopt into their home care regime to optimize daily mechanical plaque control, thus to help prevent local sequelae in the gingiva and periodontium, and help minimize broader inflammatory effects that can become intransigent and require significant dental or medical intervention. While plaque control via manual means is effective, power tooth brushing was borne out of the idea that there was room to improve. The brush head of a Philips Sonicare toothbrush sweeps at a frequency of 31,000 brush strokes per minute, it has features that prompt a thorough brushing encounter of all tooth surfaces for the dental professional-recommended two-minute period, and it requires no specific user technique in order to be effective; the brush head has only to be placed and glided across the gingival margin. Manual tooth brushing inherently lacks these features and is entirely dependent on the user to comply with practitioner

instructions and recommendations.

Since its release to market, the Philips Sonicare portfolio has undergone a sustained cadence of innovation.[18-21] The innovation pipeline is specifically focused on efforts that aid the user in developing successful compliant habits while improving on the efficacy of plaque control, safely. The Philips Sonicare DiamondClean was one such innovation, where improvements in the brush head manufacturing process opened the technical design space in terms of trim, tufting pattern, and density of the bristle field. The resultant DiamondClean brush head has 43% more bristles than its predecessor model, the ProResults brush head. As a result, the combined effect of the novel bristle configuration, operating within the high frequency range (225-280 Hz) of Philips Sonicare power toothbrushes, was expected to impart a significant benefit in helping users achieve and maintain oral health.

The current clinical trial was conducted to evaluate and confirm that the design changes on the DiamondClean standard brush head had the intended clinical effect; namely, that mechanical plaque removal and the associated hallmarks of gingival inflammation were improved relative to a manual tooth brushing control within four weeks of use.

Materials and Methods

Study Description and Objectives

This was a prospective, randomized, parallel, single-blind study designed to compare the ability of the Philips Sonicare DiamondClean power toothbrush and the ADA Reference manual toothbrush (MTB) to reduce plaque, gingival bleeding, and gingival inflammation of routine manual toothbrush users. An ADA reference manual toothbrush was selected as a control device. Safety was assessed by characterizing oral tissue status as well as effects on restorations.

This study was conducted at University Park Research Center in Ft. Wayne, IN, USA, an independent clinical research site. The study approved by the US IRB (approval U.S.IRB2011UPRC/01) was conducted in a manner consistent with the applicable US FDA regulatory statutes, the ICH E6 and E8 Guidelines, with all aspects of study conduct rooted in the ethical principles described in the WHO Declaration of Helsinki.[22]

Efficacy and Safety Measurements

Efficacy was evaluated by examiners trained in the visual assessment of plaque and gingivitis per accepted and standard visual clinical metrics. In this study, the following measurement methods were utilized: the Lobene and Soparker Modified Plaque Index[23,24] (MPI), the Modified Gingival Index[25] (MGI), and the Gingival Bleeding Index[26] (GBI). Table I presents the scale and description of the associated scores, per Index. There were two study examiners, with a single examiner assigned to perform MGI evaluations for all subjects at all visits and another examiner assigned to perform MPI and GBI evaluations for all subjects at all visits. Safety was assessed by oral tissue examination, by visual inspection and charting of restorations, and by subject report per home diary notecard.

Enrollment and Randomization

Following Informed Consent, subjects were screened for study eligibility. The accepted study population fit the following profile: age 18–70 years, in generally good health, routine manual toothbrush user, exhibiting mild to moderate gingivitis with a GBI of > 1 on at least 20 sites, MPI of > 1.8 assessed 3–6 hours since last brushing, and a non-smoker. Subjects with severe gingivitis, moderate to severe chronic periodontal disease, insulin-dependent diabetes, who were pregnant or nursing, had heavy deposits of calculus, intercurrent use of tooth bleaching trays, or who had orthodontic brackets or extensive crown or bridge work were excluded from participation in the study.

Following eligibility determination, subjects continued in the study to complete Baseline evaluations, including the characterization of restorations for subsequent safety tracking. Subjects were then randomly assigned to use either the DiamondClean power toothbrush or an ADA reference manual toothbrush, twice daily, for a home-use period of four weeks. Randomization was balanced for gender. The study examiners were blinded to the randomization assignment of all subjects to minimize bias.

All randomized subjects were dispensed Crest® Cool Mint Gel (Procter & Gamble, Cincinnati, OH, USA) fluoride-containing dentifrice to use with the assigned toothbrush, and received a diary card for compliance tracking and safety reporting. The use of any other oral hygiene products during the home-use period was prohibited. Subjects were

Table I

Scoring Methodology for Efficacy Metrics; Plaque, Gingival Inflammation and Gingival Bleeding

Lobene and Soparker Modified Plaque Index, six sites per tooth, excluding 3rd molars					
0	1	2	3	4	5
No plaque	Separate flecks of plaque at the gingival margin	A thin continuous band of plaque (up to 1mm) at the cervical margin of the tooth	A band of plaque wider than 1 mm but covering less than 1/3 of the crown of the tooth	Plaque covering at least 1/3 but less than 2/3 of the crown of the teeth	Plaque covering 2/3 or more of the tooth
Modified Gingival Index, two sites per tooth, excluding 3rd molars					
0	1	2	3	4	N/A
Absence of inflammation	Mild inflammation, slight change in color, little change in texture of any portion of but not the entire margin or papillary gingival unit	Mild inflammation but involving the entire margin or papillary unit	Moderate inflammation; glazing, redness, edema and/or hypertrophy of margin or papillary unit	Severe inflammation; marked redness, edema and/or hypertrophy or marginal or papillary gingival unit, spontaneous bleeding, congestion or ulceration	
Gingival Bleeding Index, two sites per tooth, excluding 3rd molars					
0	1	2	3	N/A	N/A
No bleeding	Bleeding on gently probing	Bleeding appears immediately upon gently probing	Spontaneous bleeding which is present prior to probing		

removed from the study in the event of an emergent need for oral care or other contraindicating medical or dental issue that stood to significantly affect compliance to the assigned study regimen.

Subjects returned to the clinic at Week 2 (± 2 days) and at Week 4 (± 2 days) to repeat the efficacy evaluations of MPI, MGI, and GBI, as well as for safety assessments. All subjects underwent efficacy evaluations with the same blinded examiners as performed at the Baseline visit. An outline of study visits and associated procedures is shown in Figure 1.

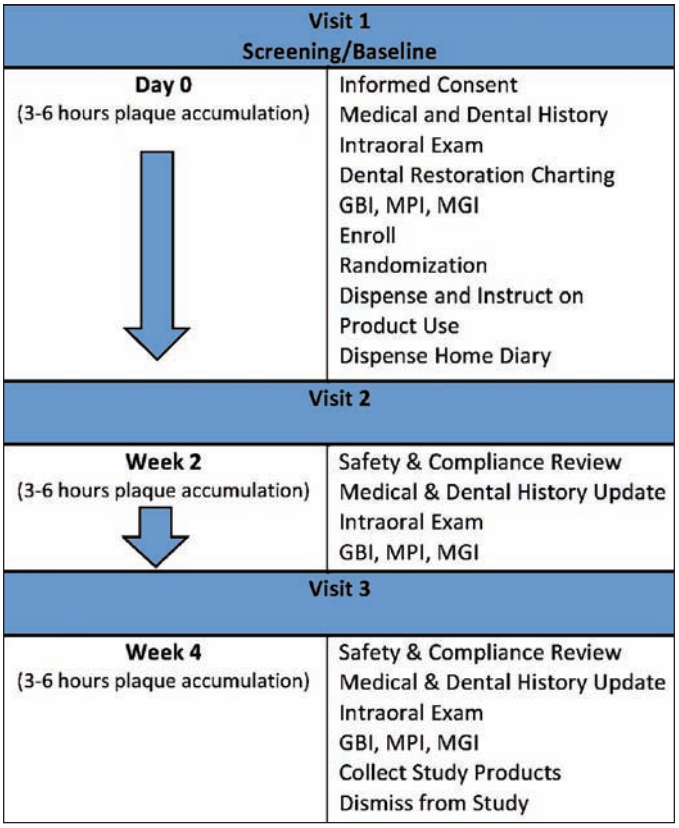

Figure 1. *Study visit flow diagram.*

Statistical Methods

Sample Size Determination. Based on the results of prior studies comparing Sonicare power versus manual toothbrushes,[18,20] a sample size of 70 subjects per group was necessary to detect a difference in GBI of 0.10 between products, with a statistical power of 90%. This power calculation assumed a common standard deviation of 0.18 for each treatment group, as well as a Type I error rate of 0.05.

General Methods. Unless otherwise noted, continuous variables were summarized using the number of non-missing observations, mean, standard deviation, median, minimum, and maximum; categorical variables were summarized using the frequency count and the percentage of subjects in each category. Subjects were grouped according to the treatment received. The efficacy measures for this study were the reduction in plaque, gingivitis score, and bleeding sites from Baseline to Week 4. Gingivitis and plaque score were calculated at Baseline and Week 4 as the sum of all evaluable sites divided by the number of evaluable sites. The number of bleeding sites was based on the number of sites with a GBI score greater than or equal to one. Outcome was expressed as the raw average score for a subject, as a reduction from Baseline (Baseline minus post Week 4 of home use), and as percent reduction calculated as the reduction in the score divided by the Baseline score times 100.

Statistical analysis was performed for the modified intent to treat (mITT) population using a mixed model with the Baseline score as a covariate. The mITT population included all randomized subjects with both a Baseline and an endpoint response. Least squares (LS) means, standard errors (SE) of the means, and 2-sided 95% Confidence Intervals (CI) were presented. The analysis presented here displays comparisons between the treatment groups as performed using the appropriate F-Test. No adjustment was performed for multiple endpoints.

Results

Demographics

The mean (SD) age for all evaluable subjects was 42.1 (12.10) years. A total of 72 subjects were enrolled and randomized to DiamondClean, of which 70 subjects had post-treatment efficacy results. For the manual toothbrush group, 72 subjects were enrolled and randomized, 72 had post-treatment efficacy results. Ninety-one of the evaluable subjects were female, 51 were male. Table II presents a summary of key demographics of study participants.

Table II
Demographic Characteristics

Characteristic	Category	MTB	DiamondClean	Total	p-value
Age (yrs)	No. Subjects	72	70	142	0.346
	Mean (SD)	43.1 (12.00)	41.1 (12.30)	42.1 (12.10)	
	Median	44	40	41.5	
	Min.-Max	(22, 67)	(20, 70)	(20, 70)	
Gender	Female	46 (63.9)	45 (64.3)	91 (64.1)	1.000
	Male	26 (36.1)	25 (35.7)	51 (35.9)	

Compliance

Subjects enrolled in this study were reported as highly compliant with the assigned study procedures. There were a total of five protocol deviations reported in the entire study; three of these were reported in the DiamondClean group and two in the manual toothbrush group. The reported deviations were minor, where corrective action was reviewed with the subject at the study site and no subjects were removed from study as a result of significant non-compliance.

Efficacy

Gingival Bleeding Index. The primary efficacy objective of the study was to compare the ability of the DiamondClean power toothbrush and the ADA Reference manual toothbrush (MTB) to reduce gingivitis as measured by gingival bleeding index (GBI) after four weeks of use. At the Baseline visit, the LS mean (SE) GBI, number of bleeding sites, for DiamondClean was 28.5 (1.13) and 29.7 (1.12) for MTB ($p = 0.4232$).

At the two-week time point, the LS mean (SE) for GBI, number of bleeding sites, for DiamondClean was 14.1 (0.92) and 24.2 (0.91) for MTB, ($p < 0.0001$). Expressed as percent reduction versus Baseline, this is a 52.2% (3.19%) reduction for DiamondClean, and 17% (3.14%) for MTB.

For the time point corresponding to the primary objective at Week 4, the LS mean (SE) outcome was 12.4 (0.89) for DiamondClean and

20.0 (0.88) for MTB ($p < 0.0001$). Expressed as a percent reduction versus Baseline, this is 57.4% (3.06%) for DiamondClean and 31.4% (3.04%) for MTB.

Table III presents model estimates for LS mean GBI scores for Baseline, Week 2, and Week 4, and LS mean GBI percent reduction from Baseline for the two study groups. A line plot of LS mean (SE) percent reduction from Baseline for GBI is presented in Figure 2.

Table III
Least Squares Mean (SE), Gingival Bleeding Index, Baseline, Week 2, Week 4

Study Visit	Variable	MTB	DiamondClean	p-value
Baseline				
	Number of Bleeding Sites	29.7 (1.12)	28.5 (1.13)	0.4232
	Gingival Bleeding Index (GBI)	0.45 (0.02)	0.42 (0.02)	0.3083
	Sites Bleeding (%)	30 (1.11)	28.7 (1.12)	0.3980
Week 2 (Day 14)				
	Number of Bleeding Sites	24.2 (0.91)	14.1 (0.92)	<0.0001
	Reduction in Sites of Gingival Bleeding (%)	17 (3.14)	52.2 (3.19)	<0.0001
	Gingival Bleeding Index (GBI)	0.36 (0.01)	0.19 (0.01)	<0.0001
	Percent Gingivitis Reduction	15.2 (3.62)	54 (3.67)	<0.0001
	Sites Bleeding (%)	24.3 (0.91)	14 (0.92)	<0.0001
Week 4 (Day 28)				
	Number of Bleeding Sites	20 (0.88)	12.4 (0.89)	<0.0001
	Reduction in Sites of Gingival Bleeding (%)	31.4 (3.04)	57.4 (3.06)	<0.0001
	Gingival Bleeding Index (GBI)	0.29 (0.01)	0.16 (0.01)	<0.0001
	Percent Gingivitis Reduction	31.8 (3.34)	61.1 (3.37)	<0.0001
	Sites Bleeding (%)	20.1 (0.88)	12.3 (0.88)	<0.0001

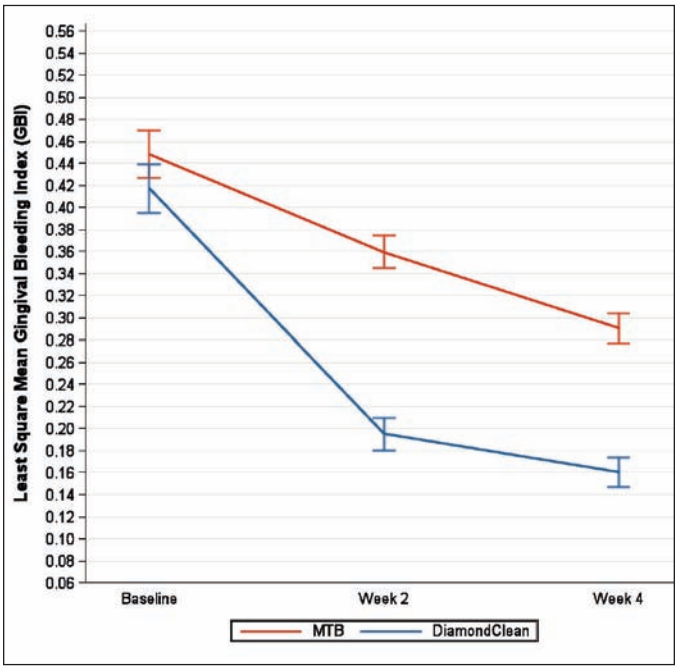

Figure 2. *Least Squares mean (SE) for GBI overall at Baseline, Week 2, Week 4*

Modified Gingival Index. At the Baseline visit, LS mean (SE) for MGI for DiamondClean was 2.08 (0.05) and 2.14 (0.05) for MTB ($p = 0.3660$). At Week 2, MGI was 1.6 (0.03) for DiamondClean and 1.83 (0.03) for MTB ($p < 0.0001$). Expressed as a percent reduction versus Baseline, this is a 24.5% (1.7) reduction for DiamondClean and 13.7% (1.6) for MTB.

At Week 4, LS mean (SE) for MGI for DiamondClean was 1.57 (0.04) and 1.71 (0.04) for MTB ($p = 0.0106$). Expressed as a percent reduction versus Baseline, this is a 25.5% (1.9) reduction for DiamondClean and 19.1% (1.9) for MTB.

Table IV presents model estimates for LS mean MGI scores for Baseline, Week 2, and Week 4, and LS mean MGI percent reduction from Baseline for the two study groups. A line plot of LS mean (SE) percent reduction from Baseline for MGI is presented In Figure 3.

Table IV
Summary Statistics, Least Squares Mean (SE), Modified Gingival Index

Study Visit	Variable	MTB	DiamondClean	p-value
Baseline	LS Mean (SE)	2.14 (0.05)	2.08 (0.05)	0.3660
Week 2	LS Mean (SE)	1.83 (0.03)	1.6 (0.03)	<0.0001
	Change from Baseline to Week 2	0.28 (0.03)	0.51 (0.03)	<0.0001
	% Change from Baseline to Week 2	13.7 (1.6)	24.5 (1.7)	<0.0001
Week 4	LS Mean (SE)	1.71 (0.04)	1.57 (0.04)	0.0106
	Change from Baseline to Week 4	0.39 (0.04)	0.53 (0.04)	0.0106
	% Change from Baseline to Week 4	19.1 (1.9)	25.5 (1.9)	0.0213

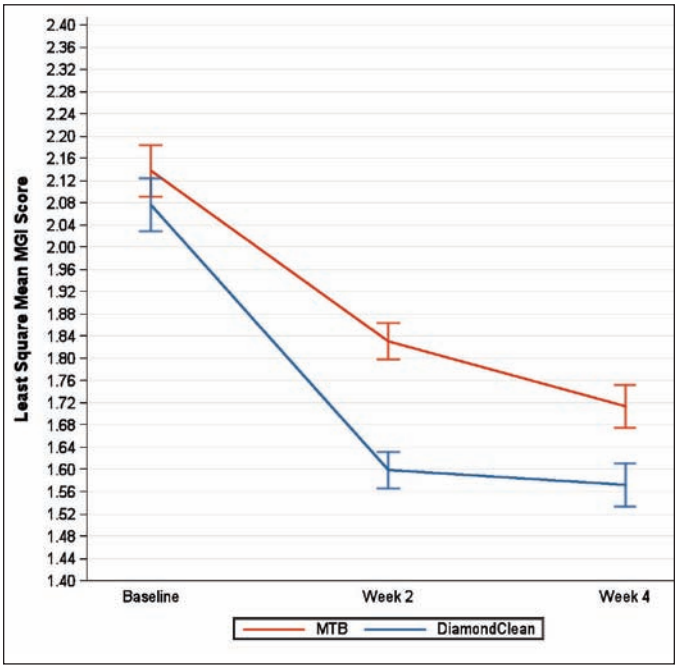

Figure 3. *Least Squares mean (SE) for overall MGI Score at Baseline, Week 2, Week 4*

Modified Plaque Index. At the Baseline visit, the LS mean (SE) MPI score for DiamondClean was 2.77 (0.05) and 2.85 (0.05) for MTB ($p = 0.2481$). At Week 2, MPI was 1.93 (0.04) for DiamondClean and 2.7 (0.04) for MTB ($p < 0.0001$). Expressed as a percent reduction versus Baseline, this is a 31.4% (1.6) reduction

for DiamondClean and 3.8% (1.6) for MTB.

At Week 4, LS mean (SE) for MPI for DiamondClean was 1.84 (0.05) and 2.58 (0.05) for MTB ($p < 0.0001$). Expressed as a percent reduction versus Baseline, this is a 34.9% (1.8) reduction for DiamondClean and 8.0% (1.7) for MTB.

Table V presents model estimates for LS mean MPI scores for Baseline, Week 2, and Week 4, and LS mean MPI percent reduction from Baseline for the two study groups. A line plot of LS mean (SE) percent reduction from Baseline for MPI is presented in Figure 4.

Table V
Summary Statistics, Overall Least Squares Mean (SE), Modified Plaque Index

Study Visit	Variable	MTB	DiamondClean	p-value
Baseline	LS Mean (SE)	2.85 (0.05)	2.77 (0.05)	0.2481
Week 2	LS Mean (SE)	2.7 (0.04)	1.93 (0.04)	<0.0001
	Change from Baseline to Week 2	0.11 (0.04)	0.88 (0.04)	<0.0001
	%Change from Baseline to Week 2	3.8 (1.6)	31.4 (1.6)	<0.0001
Week 4	LS Mean (SE)	2.58 (0.05)	1.84 (0.05)	<0.0001
	Change from Baseline to Week 4	0.23 (0.05)	0.96 (0.05)	<0.0001
	%Change from Baseline to Week 4	8.0 (1.7)	34.9 (1.8)	<0.0001

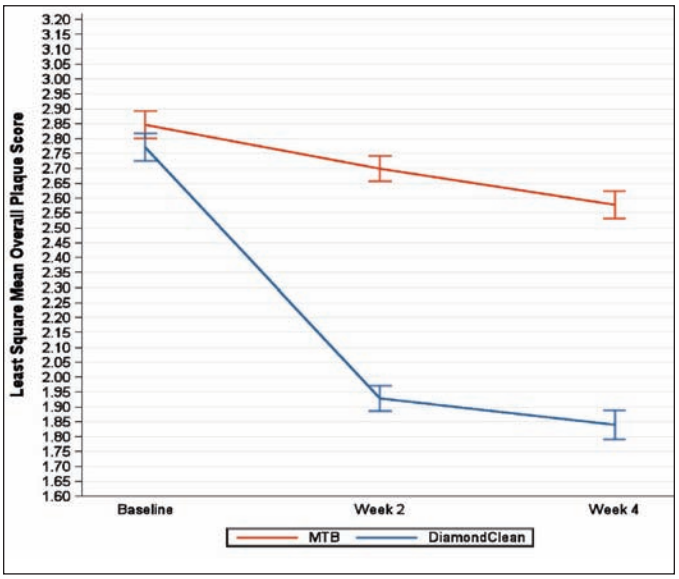

Figure 4. *Least Squares mean (SE) for Overall MPI Score at Baseline, Week 2, Week 4*

Safety

There were eight adverse events reported by three subjects during the study. Of these, five events were reported by one subject in the DiamondClean group. These five events were deemed related to the study product by the investigator and the subject was removed from study. The three events among the other two subjects (one in the manual toothbrush group, one in the DiamondClean group) were deemed unrelated to study products. There were no safety events on restorations reported in either treatment group during the study.

Discussion

This study was conducted to evaluate the extent to which the Philips Sonicare DiamondClean power toothbrush affected the gingival and plaque status of subjects following a period of home use. A standard manual tooth brushing control was selected for comparison in order to prospectively explore the magnitude of the difference that introducing DiamondClean into a user's home care regime may have on these hallmarks of oral health. The results clearly indicate that the use of DiamondClean reduces supragingival plaque, gingival inflammation, and gingival bleeding significantly better than manual brushing alone within a home-use period of four weeks.

It is noted that the oral health benefits following the implementation of power tooth brushing are already apparent following the first two weeks of home use. For the primary efficacy variable, gingival bleeding, the mean number of bleeding sites for the Sonicare group falls below the level of mild-to-moderate gingivitis established by the study entry criteria of > 20 sites by the Week 2 visit. For the MTB group, the number of bleeding sites only reaches this value at Week 4. Similar trends were also observed for the MGI and MPI study endpoints, with smaller reductions for the MTB group at Week 4 than what is observed for the Sonicare group at Week 2. This indicates that not only does the implementation of power tooth brushing effectively reduce plaque to help bring patients from the transitory state of gingivitis back to health, but can do so following a relatively short period of use.

Although *in vitro* work and pilot studies indicated the DiamondClean product used in the study reported here was safe on oral tissues, there was particular attention paid in this study, the first large clinical trial conducted using the DiamondClean brush head, on the effect of the novel technology on dental restorations, both functional and cosmetic. Thus, the study was designed to specifically characterize the restoration profile for each subject, including porcelain and metal crowns, veneers, and alloy or composite restorations. In total, there were 116 charted restorations in the Sonicare group and 137 in the manual tooth brushing group. As there were no subject-reported or examiner-observed events indicating adverse effects on restorations, DiamondClean was found safe for use in this population.

This study corroborates findings from other studies,[18-21] as well the most recent systematic review,[27] in which the use of a power toothbrush was compared to a manual toothbrush and was shown to be statistically superior at reducing plaque and improving the gingival status of study subjects. As gingivitis is readily measurable and is reversible, it is an important marker of the success of an intervention intended to improve oral health in a meaningful way for patients.

As the knowledge base of scientific evidence detailing the etiology and pathology of oral and associated systemic disease expands, it is incumbent upon the dental practitioner to engage and empower patients with tools and information that foster success in daily plaque management. Beyond the physical sensation of the presence of plaque biofilm on tooth surfaces, readily apparent to the patient, there is a complex community of microbes that initiate a cascading response of possible states of progression into decay and disease. The containment of that response to health-associated states is the goal of successful daily plaque control, and it is here where public health, practitioner, industry, and scientific efforts must come together to innovate and educate. Effective and meaningful therapies, in the hands of patients at home, will be where the greatest public health impact can occur. In such cases of innovation, randomized, controlled clinical trials are necessary to inform the progression of evidence-based recommendations for daily oral care.

Acknowledgment: This study was sponsored by Philips Oral Healthcare.

Conflict of Interest: MD, MW, SS, and WJ are employees of Philips, maker of the Sonicare powered toothbrush that was tested in this study. MP, KM, and JM are employees of an independent clinical research site. No external funding was received for this study.

For correspondence with the authors of this paper, contact Dr. Marcia Delaurenti —Marcia.Delaurenti@Philips.com.

References

1. Socransky SS, Haffajee AD. Periodontal microbial ecology. *Periodontol 2000* 2005;38:135-87.
2. Kroes I, Lepp PW, Relman DA. Bacterial diversity within the human subgingival crevice. *Proc Natl Acad Sci USA* 1999;96:14547-52.
3. Mason M, Nagaraja H, Camerlengo T, Joshi V, Kumar P. Deep sequencing identified ethnicity-specific bacterial signatures in the oral microbiome. *PLoS One* 2013;8:e77287.
4. Page RC, Offenbacher S, Schroeder HE, Seymour GJ, Kornman KS. Advances in the pathogenesis of periodontitis; summary of developments, clinical implications and future directions. *Periodontol 2000* 1997;14: 216-48.
5. Paster BJ, Boches SK, Galvin JL, Ericson RE, Lau CN, Levanos VA, Sahasrabudhe A, Dewhirst FE. Bacterial diversity in human subgingival plaque. *J Bacteriol* 2001;183:3770-83.
6. Kumar PS, Griffen AI, Baron JA, Paster BJ, Moeschberger MI. New bacterial species associated with chronic periodontitis. *J Dent Res* 2003;83:338-44.
7. Listgarten MA. Structure of the microbial flora associated with periodontal health and disease in man. A light and electron microscopic study. *J Periodontol* 1976;47:1-18.
8. Shchipkova AY, Nagaraja HN, Kumar PS. Subgingival microbial profiles of smokers with periodontitis. *J Dent Res* 2010;89:1247-53.
9. Mason MR, Preshaw PM, Nagaraja HN, Dabdoub SM, Rahman A, Kumar PS. The subgingival microbiome of clinically healthy and current never smokers. *The ISME J* 2015;9:268–72.
10. Kumar PS, Matthews C, Joshi V, de Jager M, Aspiras M. Tobacco smoking affects bacterial acquisition and colonization in oral biofilms. *Infect Immun* 2011b;79:4730-8.
11. Marsh PD, Bradshaw DJ. Dental plaque as a biofilm. *J Indust Microbiol* 1995;15:169-75.
12. Li X, Kolltveit KM, Tronstad I, Olsen I. Systemic diseases caused by oral infection. *Clin Microbiol Rev* 2000;13:547-58.
13. Mattila KJ, Valtonen VV, Nieminen MS, Asikainen S. Role of infection as a risk factor for atherosclerosis, myocardial infarction, and stroke. *Clin Infect Dis* 1998;26:719-34.
14. Mattila KJ, Dental infections as a risk factor for acute myocardial infarction. *Eur Heart J* 1993;14(Suppl K):51-3.
15. Söder B, Yakob M, Meurman JH, Andersson LC, Klinge B, Söder PÖ. Periodontal disease may associate with breast cancer. *Breast Cancer Res Treat* 2011;127:497-502.
16. Kshirsagar A, Craig R, Moos KL, Beck JD, Offenbacher S, Kotanko P, Klemmer PJ, Yoshino M, Levin NW, Yip JK, Almas K, Lopovici EM, Usvay LA, Falk RJ. Periodontal disease adversely affects the survival of patients with end-stage renal disease. *Kidney Int* 2009; 75:746-50.
17. Taylor JJ, Preshaw PM, Lalla E. A review of the evidence for pathogenic mechanisms that may link periodontitis and diabetes. *J Clin Periodontol* 2013;40(Suppl 14):S113-34.
18. Holt J, Sturm D, Master A, Jenkins W, Schmitt P, Hefti A. A randomized, parallel-design study to compare the effects of the sonicare flexcare and the Oral-B P40 manual toothbrush on plaque and gingivitis. *Compend Contin Educ Dent* 2007;28:35-41.
19. Barlow AP, Zhou X, Roberts J, Colgan P. Effect of a novel integrated power toothbrush and toothpaste oral hygiene system on gingivitis. *Compend Contin Educ Dent* 2004;25:15-20.
20. Moritis JK, Delaurenti M, Johnson M, Berg J, Boghosian A. Comparison of the sonicare elite and a manual toothbrush in the evaluation of plaque reduction. *Am J Dent* 2002;15(Spec Iss):23B-5.
21. Kugel G, Boghosian A. Impact of the sonicare toothbrush on plaque and gingivitis. *Compend Contin Educ Dent* 2002;23:7-10.
22. *World Medical Association Declaration of Helsinki*. Available from: http://www.wma.net/en/30publications/10policies/b3/17c.pdf [accessed Oct 2016].
23. Lobene RR, Soparkar PM, Newman MB. Use of dental floss. Effect on plaque and gingivitis. *Clin Prev Dent* 1982;4:5-8.
24. Quigley GA, Hein JW. Comparative cleansing efficiency of manual and power brushing. *J Am Dent Assoc* 1962;65:26-9.
25. Lobene RR, Weatherford T, Ross NM, Lamm RA, Menaker L. A modified gingival index for use in clinical trials. *Clin Prev Dent* 1986;8:3-6.
26. Van der Weijden F, Timmerman MF, Nijboer A, Reijerse E, Van der Velden U. Comparison of different approaches to assess bleeding on probing as indicators of gingivitis. *J Clin Periodontol* 1994;21:589-94.
27. Yaacob M, Worthington H, Deacon S, Deery C, Walmsley A, Robinson P, Glenny A. Powered versus manual toothbrush for oral health. *Cochrane Database Syst Rev* 2014;(6):CD002281.

An Evaluation of Plaque and Gingivitis Reduction Following Home Use of Sonicare FlexCare Platinum with Premium Plaque Control Brush Head and a Manual Toothbrush

Wendy Jenkins, BA Sonia Souza, PhD Marilyn Ward, DDS Jodi Defenbaugh, BS

Philips Healthcare
Bothell, WA, USA

Kimberly R. Milleman, RDH, BSEd, MS Jeffery L. Milleman, DDS, MPA

Salus Research
Ft. Wayne, IN, USA

Abstract

- **Objective:** To assess the effect of the Philips Sonicare FlexCare Platinum with Premium plaque control brush head on gingival inflammation, bleeding, and supragingival plaque reduction following a six-week period of home use compared to a manual toothbrush.
- **Methods:** This was a randomized, single-blind, parallel-design clinical trial. Subjects included in the study were routine manual toothbrush users who were generally healthy non-smokers, aged 18–65 years, with mild to moderate gingivitis. Subjects with advanced periodontal disease, excessive gingival recession, and heavy deposits of calculus or rampant decay were excluded from the study. Eligible participants were dispensed either Philips Sonicare FlexCare Platinum with Premium plaque control brush head (PC), or an ADA Reference manual toothbrush (MTB) for twice-daily home oral hygiene procedures for six weeks. Efficacy measures included the Lobene and Soparker Modification of Quigley and Hein Plaque Index (MPI), the Modified Gingival Index (MGI), and Gingival Bleeding Index (GBI). Safety was evaluated by oral examination and subject report. Efficacy and safety were assessed at Baseline, and at two and six weeks following product home use.
- **Results:** Of 154 subjects randomized, 143 subjects completed the study. For the primary endpoint, MGI at Week 2, statistically significantly larger reductions in MGI were observed for PC versus MTB, $p < 0.0001$. The adjusted mean reduction and standard error estimates (SE) for MGI, expressed as percent reduction versus Baseline to Week 2, were 41.73% (2.00%) for PC and 7.38% (2.02%) for MTB. Statistically significant differences were also observed for MPI and GBI at Week 2, and for all metrics at Week 6.
- **Conclusion:** Philips Sonicare FlexCare Platinum with Premium plaque control brush head statistically significantly reduces gingival inflammation, gingival bleeding, and plaque following two and six weeks of home use, compared to manual tooth brushing alone.

(J Clin Dent 2017;28(Spec Iss A):A7–12)

Introduction

The interface between a tooth, the bacteria-laden plaque that coats and surrounds its surface, and the adjacent gingivae is a site of dynamic activity.[1] It is one of several sites in the body where the ecology of the external environment interacts with that of the host and is, thus, a focal point for the initiation of the communication signals that up- and down-modulate the mediators that influence oral health and disease.[2,3]

The presence of inflamed gingival tissue and gingival bleeding are the clinically observable hallmarks of tissue in a potentially transition state, where adequate intervention can restore health or where disease can develop, putting the tooth at risk of eventual loss.[4,5] Taking a broader view of human health, there is mounting research that associates an inflammatory environment in oral tissues with inflammatory conditions elsewhere in the body.[6-10]

The prevention of events that have their etiology in inflammatory processes at this interface between gingivae and teeth lies largely in the hands of patients; their lifestyle choices, compliance to professional intervention and recommendations, their dietary habits, and home oral care routine all contribute to oral health status. Providing patients with the tools to be successful in their prevention and management efforts at home have spurred the development of a spectrum of technologies and medicaments. As a technology innovator in this space, Philips Sonicare focused design efforts on developing a brush head for its power toothbrush platform where the brush head benefits were specifically targeted to help patients achieve gingival health; a very important, symptomatically expressive site where the dynamic physiology driving healthy and disease states actively happens.

The current study was undertaken to evaluate the efficacy and safety of the Philips Sonicare FlexCare Platinum and Premium plaque control* brush head (Philips Healthcare, Bothell, WA, USA) in order to assess its effects on gingival health and supragingival plaque reduction. The Premium plaque control brush head is notable in its distinction from others in the Philips Sonicare portfolio in that it was engineered to achieve efficacy under a wide range of user-load. This innovative brush head design is the first of its kind to use a thermoplastic elastomer in which free-standing tufts are molded. This enables the bristle tufts to move freely relative to one another, such that when one tuft is inhibited from movement by entrapment or excess force, the neighboring tufts can still move. This creates a condition where the brush head can be effective under load conditions that vary sig-

nificantly. This includes conditions that differ from patient to patient, but also within the same patient where a number of factors influence thorough coverage in a given brushing encounter. Such factors include variation in the levels of force applied based on the hand used to brush, the position of the toothbrush relative to an individual's oral anatomy, the dexterity with which the patient brushes, and the habits borne out of years of performing this seemingly mundane task.

In addition, the coupling of high-frequency, high-amplitude sonic motion initiated by the Philips Sonicare drivetrain with the elastomer-anchored bristle tufts transfers energy more effectively through the brush head than other brush heads, thus increasing the arc of motion through which the bristles move. As a result, the bristles sweep over an amplified surface area, providing more contact with tooth and gum structures during brushing. Further, this elastomer, being a softer polymer, has a gentler in-mouth feel that users may prefer over hard plastics.

Together, these design features were intended to aid patients in achieving a comprehensive hygiene encounter by avoiding the pitfalls of missed spots, sites of irregular and suboptimal mechanical plaque removal. The Premium plaque control brush head can dynamically conform to hard and soft anatomical structures, particularly along the gingival margin, and can still operate effectively in the presence of complex oral anatomy or variations in user dexterity. Thus, everyday usage of the brush head stands to impact the microenvironments that are generally susceptible to the effects of a plaque ecology that favors pathogenic transition as a consequence of irregular mechanical plaque removal. As the regrowth of harmful plaque bacteria in these microenvironments is diminished, the symptomatic expression of gingivitis was postulated to follow suit.

Thus, the current clinical trial was conducted to evaluate whether the Philips Sonicare FlexCare Platinum with Premium plaque control brush head achieved the desired effect of reducing plaque, with resultant reduction in gingival inflammation and gingival bleeding observed in parallel. A standard of care manual toothbrush (MTB) was selected as the control device for comparison.

(*Note, the Premium plaque control brush head was formerly called AdaptiveClean, and is known as Premium plaque defense in some countries.)

Materials and Methods

Study Design and Objectives

This was a prospective, randomized, parallel, single-blind clinical trial conducted in generally healthy volunteers aged 18–65 years old. The study was approved by the US Investigational Review Board (approval, U.S.IRB2015SRI/07) and was conducted in a manner consistent with applicable US FDA statutes, ICH GCP Guidelines, with the ethical treatment of human subjects rooted in the principles outlined in the World Medical Association Declaration of Helsinki.[11]

The primary objective of the study was to compare the effect of brushing with Premium plaque control versus a manual toothbrush on gingival inflammation (MGI) following a two-week period of product home use. Secondary objectives included comparisons of the effect of each product on MGI following six weeks of use, comparisons between products and their respective effects on gingival bleeding and supragingival plaque reduction following two and six weeks of use, and the safety of the study products.

Data were collected at three study visits: Baseline (Visit 1), Week 2 ± 2 days (Visit 2) and Week 6 ± 2 days (Visit 3). Subjects observed a three- to six-hour plaque accumulation period prior to all study visits. An outline of study visits with the procedures at each visit is provided in Figure 1.

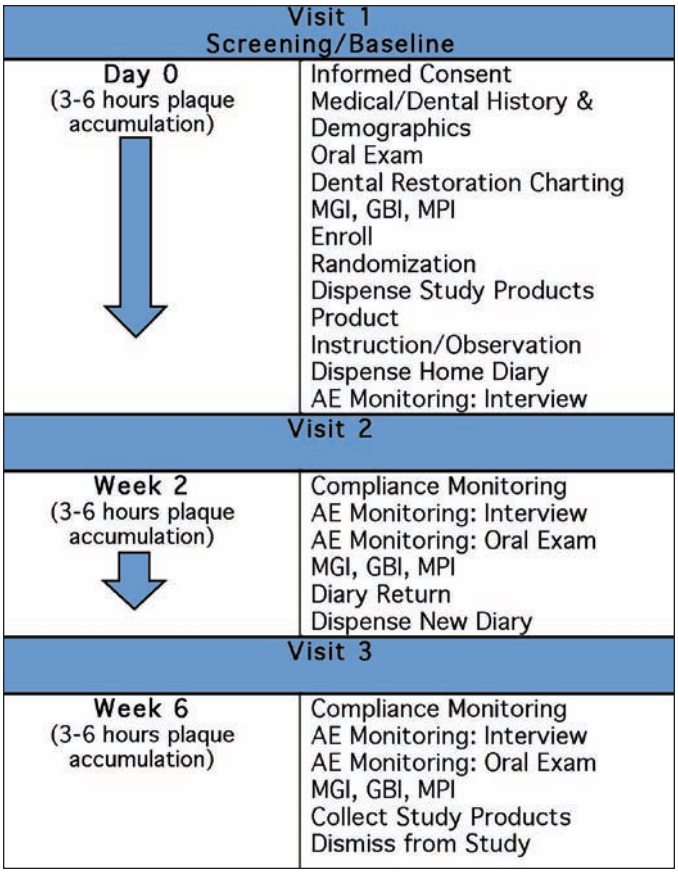

Figure 1. *Study visits and the procedures at each visit.*

Subjects

The eligibility profile of the accepted study panel included the following key criteria: able to voluntarily provide Informed Consent; non-smoker; routine manual toothbrush user; Gingival Bleeding Index[12] (GBI) of ≥ 1 on at least 20 sites; and a minimum plaque score of ≥ 1.8 per Lobene and Soparker Modified Plaque Index[13,14] (MPI) following three to six hours of plaque accumulation. Subjects were excluded in the event of intercurrent illness or course of treatment that would be unduly affected by participation in the study, use of antibiotics within four weeks of enrollment, chronic use of prescription-dose anti-inflammatory or anti-coagulant medication, advanced periodontal disease or excessive gingival recession, or the presence of orthodontic hardware.

Randomization and Study Treatment Groups

Those subjects who met the eligibility profile were enrolled and randomized. Subjects were randomized to one of two treatment groups; either Sonicare FlexCare Platinum with Premium plaque control brush head or an ADA reference manual toothbrush for the subsequent six-week home use period. Randomization was balanced for gender such that approximately equal numbers of males and females were allocated to each treatment group. All subjects received a standard fluoride-containing dentifrice to use with the assigned toothbrush, and were prohibited from using interdental cleaning aids, mouth rinse, and tooth bleaching products for the duration of the study.

Table I
Scoring Methodology for Efficacy Metrics; Plaque, Gingival Inflammation and Gingival Bleeding

Lobene and Soparker Modified Plaque Index, six sites per tooth, excluding 3rd molars					
0	1	2	3	4	5
No plaque	Separate flecks of plaque at the cervical margin	A thin continuous band of plaque (up to 1mm) at the cervical margin of the tooth	A band of plaque wider than 1 mm but covering less than 1/3 of the crown of the tooth	Plaque covering at least 1/3 but less than 2/3 of the crown of the tooth	Plaque covering 2/3 or more of the crown of the tooth
Modified Gingival Index, four sites per tooth, excluding 3rd molars					
0	1	2	3	4	N/A
Absence of inflammation	Mild inflammation, slight change in color, little change in texture of the marginal or papillary gingival unit	Mild inflammation but involving the marginal or papillary gingiva	Moderate inflammation; glazing, redness, edema and/or hypertrophy of marginal or papillary gingiva	Severe inflammation; marked redness, edema and/or hypertrophy of the marginal or papillary gingiva, spontaneous bleeding, congestion or ulceration	
Gingival Bleeding Index, four sites per tooth, excluding 3rd molars					
0	1	2	3	N/A	N/A
No bleeding	Bleeding on gently probing	Bleeding appears immediately upon gently probing	Spontaneous bleeding which is present prior to probing		

Efficacy and Safety Measurements

Efficacy was evaluated by examiners trained in the visual assessment of plaque and gingivitis per accepted and standard visual clinical metrics. The examiners were blinded to the treatment allocation of the study subjects in order to minimize bias. In this study, the following measurement methods were utilized; Lobene and Soparker Modified Plaque Index, the Modified Gingival Index[15] (MGI), and the Gingival Bleeding Index. Table I shows the scale and description of the associated scores, per Index.

Safety was assessed by oral tissue exam at each study visit and by subject report per home diary. In the event that a subject required dental or medical care in a context that could affect a safety or efficacy endpoint of the study, or which put the subject at greater risk, the participant was removed from study at the discretion of the study investigator. Compliance to the prescribed regimen was tracked by use of a diary and subject interview in clinic.

Data Capture

Study data were collected on a web-based platform with programmed logic and edit-checks. Access to the web-based system was limited by log-in credentials that matched the study role of the user. Applicable source document forms were utilized where necessary. Study data were monitored to ensure accuracy of the data set prior to any analysis. Study data were merged with the randomization schedule after database lock.

Statistical Methods

Primary Objective and Determination of Sample Size. The primary objective of the trial was to compare the reduction in gingivitis (MGI) between the two study products following two weeks of use. Based on prior studies in which Sonicare power tooth brushing was compared to manual tooth brushing, it was reasonable to assume a minimum difference of 0.14 in MGI reduction was clinically meaningful to differentiate the two treatments, with the common standard deviation (SD) of 0.3. Given this assumption, a sample size of 74 subjects per group would allow for approximately 80% power to detect a difference of 0.14 in MGI reduction between the two products using a two sided t-test at a 0.05 significance level. Similarly, this sample size would allow for detection of at least 10% difference in MGI percent reduction between the two products, assuming that the common SD was less than 20%.

Overall, a total of 156 subjects (78 subjects per group) were required to be randomized with a target to complete with 148 evaluable subjects (74 subjects per group).

Efficacy Endpoints. The efficacy indices, MGI, GBI, and MPI, at each tooth site were scored using the methodology described in Table I. A standardized collection form was used to capture these data at each study visit. For each index, three summary scores were used as efficacy endpoints. These included: the overall score, calculated as the sum of scores at all evaluable sites divided by the number of evaluable sites; reduction from Baseline, calculated as the Baseline score minus the post baseline score; and percent reduction from Baseline, calculated as the reduction in score divided by the Baseline score times 100.

All three summary scores were considered as continuous variables and summarized for the whole mouth (overall) and by region of the mouth (*i.e.*, anterior, posterior, interproximal, and posterior interproximal). Analyses were performed separately for each summary score and for each region.

General Statistical Methods. Continuous variables were summarized using the number of non-missing observations, mean, standard deviation, median, minimum, and maximum; categorical variables were summarized using the frequency count and the percentage of subjects in each category. All analyses were conducted using SAS® software (SAS Institute Inc, Cary NC, USA).

Standard subject demographics and baseline characteristics were summarized by treatment group for all randomized subjects. For continuous subject characteristics, means were compared between groups using one-way analysis of variance (ANOVA). The incidence of categorical variables was compared using a Chi-square test. The analysis of safety included all randomized subjects who were exposed to either one of the treatment products.

Efficacy Analysis. The efficacy analysis was performed on the modified intent to treat (mITT) population, which included all randomized subjects with an MGI score at Baseline and Week 2. For each efficacy endpoint (MGI, GBI, MPI) at each follow up visit, a linear model was used to estimate adjusted mean score, mean reduction in score, and

mean percent reduction for each treatment group after adjusting for the Baseline score as a covariate. Comparisons between treatment groups were performed using an F-test.

Results

Demographics

One hundred sixty-nine subjects were screened for the study, of which 154 were randomized. A total of 143 subjects completed the entire study (72 in the PC group and 71 in the MTB group). Of the 11 subjects who did not complete the study, two were removed at the discretion of the principal investigator, two were lost to follow-up, and seven chose to discontinue.

Of all randomized subjects, 111 (72.1%) were female and 43 (27.9%) were male. The mean (SD) age of subjects was 40.6 (11.5) years. There were no statistical differences in age or gender between treatment groups. Table II presents a summary of the demographics of the randomized study subjects.

Table II
Demographic Characteristics

Characteristic	Category	MTB	Sonicare + Premium Plaque Control	Total	p-value
Age (yrs)	No. Subjects	78	76	154	0.8088
	Mean (SD)	40.8 (11.7)	40.4 (11.5)	40.6 (11.5)	
	95% CI	(38.3, 43.5)	(37.8, 43.0)	(38.8, 42.5)	
	Median	42	40	40.5	
	Min.-Max	(19, 63)	(20, 64)	(19, 64)	
Gender	Female	56 (71.8%)	55 (72.4%)	111 (72.1%)	0.9368
	Male	22 (28.2%)	21 (27.6%)	43 (27.9%)	

Efficacy

Modified Gingival Index. Table III presents model estimates for adjusted mean MGI scores for Baseline, Week 2, and Week 6, and adjusted mean MGI percent reduction from Baseline for the two study groups.

At Baseline, MGI scores were balanced between the two groups. The adjusted mean (and 95% confidence interval) scores were 2.16 (2.07, 2.26) for PC and 2.27 (2.17, 2.37) for MTB; p-value = 0.1282.

For the primary efficacy endpoint following two weeks of use, the adjusted mean (95% CI) MGI scores were 1.32 (1.24, 1.40) for PC and 2.05 (1.98, 2.13) for MTB.

Following six weeks of use, the adjusted mean (95% CI) MGI scores were 1.23 (1.15, 1.31) for PC and 2.22 (2.14, 2.30) for MTB. A line plot of adjusted mean percent reduction from Baseline for MGI is presented in Figure 2. Statistical superiority was observed between PC compared to MTB ($p < 0.0001$) at both Week 2 and Week 6.

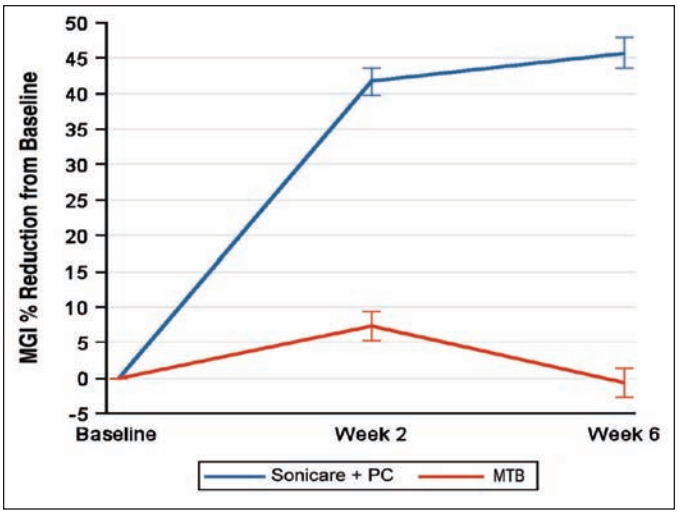

Figure 2. *Line plot of adjusted mean percent reduction in MGI by visit. Note: The vertical bars represent adjusted mean ± standard error.*

Table III
Modified Gingival Index, Adjusted Mean, Overall, at Baseline, Week 2, Week 6

Variable	Statistic	Treatment: Sonicare + Premium Plaque Control	Treatment: MTB	Total	p-value
MGI Score					
Baseline	Adjusted Mean (SE)	2.16 (0.05)	2.27 (0.05)	-0.11 (0.07)	0.1282
	95% CI	(2.07, 2.26)	(2.17, 2.37)	(-0.24, 0.03)	
Week 2	Adjusted Mean (SE)	1.32 (0.04)	2.05 (0.04)	-0.73 (0.06)	<0 .0001
	95% CI	(1.24, 1.40)	(1.98, 2.13)	(-0.85, -0.62)	
Week 6	Adjusted Mean (SE)	1.23 (0.04)	2.22 (0.04)	-0.99 (0.06)	<0 .0001
	95% CI	(1.15, 1.31)	(2.14, 2.30)	(-1.11, -0.87)	
% Reduction from Baseline					
Week 2	Adjusted Mean (SE)	41.73 (2.00)	7.38 (2.02)	34.35 (2.85)	< 0.0001
	95% CI	(37.78, 45.67)	(3.38, 11.37)	(28.71, 39.99)	
Week 6	Adjusted Mean (SE)	45.79 (2.06)	-0.71 (2.08)	46.50 (2.94)	<0 .0001
	95% CI	(41.71, 49.87)	(-4.82, 3.40)	(40.68, 52.32)	

Gingival Bleeding Index. Table IV presents model estimates for adjusted mean GBI scores for Baseline, Week 2, and Week 6, and adjusted mean GBI percent reduction from Baseline for the two study groups.

At Baseline, GBI scores were balanced between the two groups. The adjusted mean (and 95% confidence interval) scores were 0.40 (0.35, 0.45) for PC and 0.39 (0.34, 0.44) for MTB (p = 0.7934).

Following two weeks of use, the adjusted mean (95% CI) GBI scores were 0.19 (0.16, 0.22) for PC and 0.34 (0.32, 0.37) for MTB.

At Week 6, the adjusted mean (95% CI) GBI scores were 0.15 (0.13, 0.18) for PC and 0.38 (0.35, 0.41) for MTB. Figure 3 depicts these results for adjusted mean percent reduction from Baseline in a line plot. Statistical superiority was observed between PC compared to MTB ($p < 0.0001$) at both Week 2 and Week 6.

Modified Plaque Index. Table V presents model estimates for adjusted mean MPI scores for Baseline, Week 2, and Week 6, and adjusted mean MPI percent reduction from Baseline for the two study groups.

At Baseline, MPI scores were balanced between the two groups.

Table IV
Gingival Bleeding Index, Adjusted Mean, Overall, at Baseline, Week 2, Week 6

Variable	Statistic	Treatment: Sonicare + Premium Plaque Control	Treatment: MTB	Total	p-value
GBI Score					
Baseline	Adjusted Mean (SE)	0.40 (0.03)	0.39 (0.03)	0.01 (0.04)	0.7934
	95% CI	(0.35, 0.45)	(0.34, 0.44)	(-0.06, 0.08)	
Week 2	Adjusted Mean (SE)	0.19 (0.01)	0.34 (0.01)	-0.15 (0.02)	< 0.0001
	95% CI	(0.16, 0.22)	(0.32, 0.37)	(-0.19, -0.11)	
Week 6	Adjusted Mean (SE)	0.15 (0.01)	0.38 (0.01)	-0.23 (0.02)	<0 .0001
	95% CI	(0.13, 0.18)	(0.35, 0.41)	(-0.27, -0.19)	
% Reduction from Baseline					
Week 2	Adjusted Mean (SE)	47.97 (3.72)	8.64 (3.77)	39.33 (5.29)	<0 .0001
	95% CI	(40.62, 55.32)	(1.19, 16.09)	(28.86, 49.79)	
Week 6	Adjusted Mean (SE)	58.36 (3.55)	-3.14 (3.57)	61.50 (5.03)	<0 .0001
	95% CI	(51.34, 65.37)	(-10.20, 3.92)	(51.54, 71.45)	

The adjusted mean (and 95% confidence interval) scores were 2.84 (2.72, 2.95) for PC and 2.90 (2.79, 3.02) for MTB (p = 0.4159).

Following two weeks of use, the adjusted mean (95% CI) MPI scores were 1.42 (1.29, 1.54) for PC and 2.77 (2.65, 2.90) for MTB.

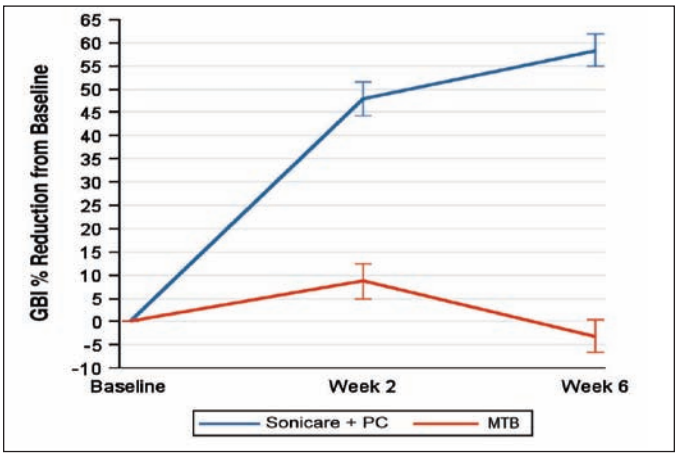

Figure 3. *Line plot of adjusted mean percent reduction in GBI by visit. Note: The vertical bars represent adjusted mean ± standard error.*

Table V
Modified Plaque Index, Adjusted Mean, Overall, at Baseline, Week 2, Week 6

Variable	Statistic	Treatment: Sonicare + Premium Plaque Control	Treatment: MTB	Total	p-value
MPI Score					
Baseline	Adjusted Mean (SE)	2.84 (0.06)	2.90 (0.06)	-0.07 (0.08)	0.4159
	95% CI	(2.72, 2.95)	(2.79, 3.02)	(-0.23, 0.10)	
Week 2	Adjusted Mean (SE)	1.42 (0.06)	2.77 (0.06)	-1.36 (0.09)	<0 .0001
	95% CI	(1.29, 1.54)	(2.65, 2.90)	(-1.54, -1.18)	
Week 6	Adjusted Mean (SE)	1.55 (0.07)	2.91 (0.07)	-1.36 (0.10)	<0 .0001
	95% CI	(1.41, 1.69)	(2.77, 3.05)	(-1.55, -1.16)	
% Reduction from Baseline					
Week 2	Adjusted Mean (SE)	50.59 (2.19)	3.08 (2.22)	47.51 (3.12)	<0 .0001
	95% CI	(46.26, 54.92)	(-1.31, 7.47)	(41.34, 53.68)	
Week 6	Adjusted Mean (SE)	46.55 (2.46)	-1.58 (2.48)	48.12 (3.50)	<0 .0001
	95% CI	(41.68, 51.42)	(-6.48, 3.33)	(41.20, 55.05)	

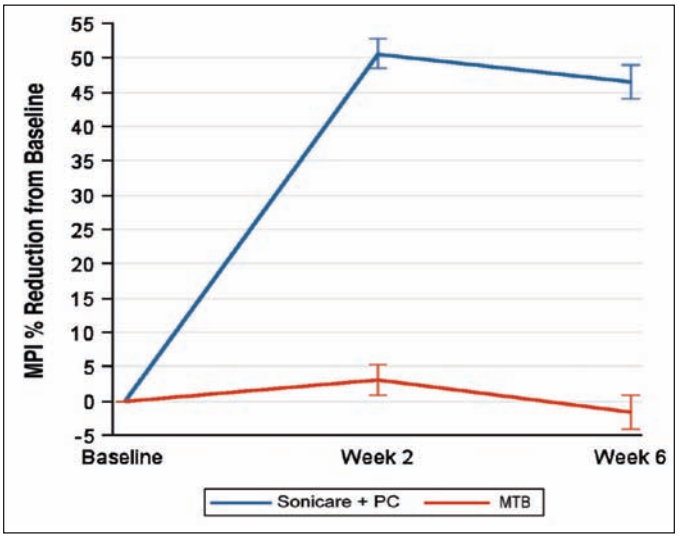

Figure 4. *Line plot of adjusted mean percent reduction in MPI by visit. Note: the vertical bars represent adjusted mean ± standard error.*

At Week 6, the adjusted mean (95% CI) MPI scores were 1.55 (1.41, 1.69) for PC and 2.91 (2.77, 3.05) for MTB. Figure 4 depicts these results for adjusted mean percent reduction from Baseline in a line plot. Statistical superiority was observed between PC compared to MTB (p < 0.0001) at both Week 2 and Week 6.

To evaluate the benefit of PC versus MTB on different regions of the mouth, particularly "hard-to-reach areas," MPI efficacy endpoints were also analyzed by sub-region of the mouth (anterior, posterior, interproximal, and posterior interproximal). Figures 5 and 6 depict

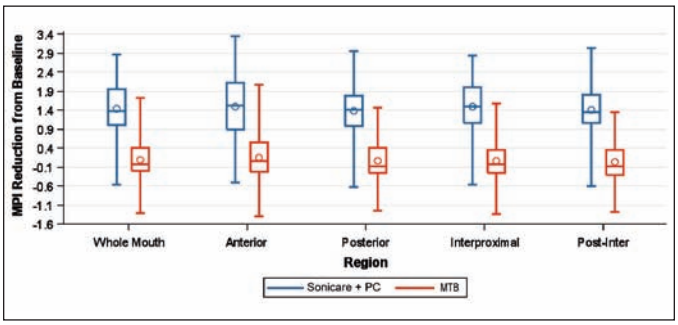

Figure 5. *Boxplot for Modified Plaque Index, reduction from Baseline to Week 2, by region. Note: the "Post-Inter" label refers to the "Posterior Interproximal" sub-region.*

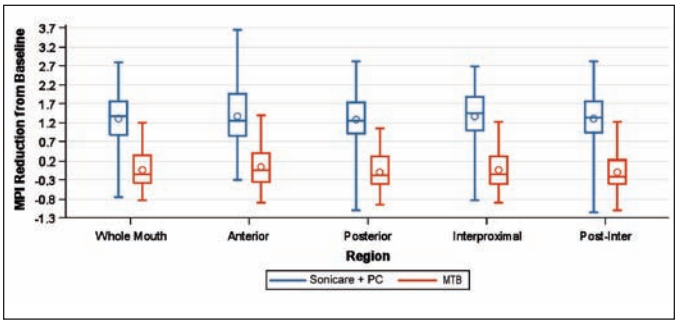

Figure 6. *Boxplot for Modified Plaque Index, reduction from Baseline to Week 6, by region. Note: The "Post-Inter" label refers to the "Posterior Interproximal" sub-region.*

the boxplot for reduction from Baseline for overall and by sub-region at Weeks 2 and 6, respectively.

Safety

Two adverse events were reported in this study. Both events (headache and generalized muscle aches) were reported in the manual toothbrush group and were assessed by the investigator to be mild in severity and unlikely related to the study. There were no serious adverse events reported.

Discussion and Conclusions

The use of Philips Sonicare FlexCare Platinum with Premium plaque control brush was shown to improve gingival health, per MGI, significantly better than a manual toothbrush control within two weeks of use. This effect was sustained, with a continuing trend of reduction observed for both tissue inflammation (MGI) and tissue bleeding (GBI) metrics at Week 6. Similar clinical effects were observed in the assessment of plaque reduction, with the power toothbrush demonstrating a significant difference as early as two weeks, and sustained at six weeks. The results observed in this study further corroborate the evidence base that powered tooth brushing is superior to manual tooth brushing in

reducing plaque and gingivitis.[16-20]

The observable clinical expression of gingivitis, inflamed tissue and bleeding, is where a practitioner's clinical focus can have an important impact on a patient's oral health. This includes appropriate intervention in the clinical setting, but also in helping patients optimize their home care regime where the opportunity to achieve and maintain oral health is in the hands of patients. The coupling of the high-frequency, high-amplitude mode of action of the Philips Sonicare drive train to the innovative design of the Premium plaque control brush head is a highly effective means of targeting this problem.

Indeed, the insight that drove the design of the Premium plaque control product came from dental professionals themselves. A common refrain in queries to the profession about how technology can improve the home care regime of patients is the everyday clinical observation that patients often have missed spots that lead to short- and long-term problems. In spite of education and recommendations to improve home care habits, patients return to the clinic with the same problem sites from visit to visit.

Thus was borne the proposition for a brush head that specifically adapted to both a patient's dental anatomy and technique, in order to target those missed spots that harbor plaque. As plaque ages, the ecological profile and associated mediators within begin to exhibit more disease-associated characteristics, and the tissues surrounding tooth structures respond accordingly.[21] By introducing a Philips Sonicare power toothbrush plus Premium plaque control brush head, the problems initiated in those missed areas stand to steadily improve. As plaque regrowth is regularly limited by effective mechanical removal, so too are the local sequelae of inflammation and bleeding in the corresponding gingivae. In reaching into problematic plaque micro-environments, the Premium plaque control brush head affords the patient an opportunity to achieve and maintain optimal oral health.

Acknowledgment: This study was sponsored by Philips Oral Healthcare.

Conflict of Interest: Source for funding: WJ, MW, SS, and JD are employees of Philips, maker of the Sonicare powered toothbrush that was tested in this study. KM and JM are employees of an independent clinical research site.

For correspondence with the authors of this paper, contact Wendy Jenkins – wendy.jenkins@philips.com

References

1. Offenbacher S, Barros SP, Singer RE, Moss K, Williams RC, Beck JD. Periodontal disease at the biofilm-gingival interface. *J Periodontol* 2007;78:1911-25.
2. Kornman KS. Mapping the pathogenesis of periodontitis: A new look. *J Periodontol* 2008;79(8 Suppl):1560-8.
3. Tatakis DN, Kumar PS. Etiology and pathogenesis of periodontal disease. *Dent Clin North Am* 2005;49:491-515.
4. Löe H, Anerud A, Boysen H, Morrison E. Natural history of periodontal disease in man. Rapid, moderate and no loss of attachment in Sri Lankan laborers 14-16 years of age. *J Clin Periodontol* 1986;13:431-45.
5. Listgarten MA, Schifter CC, Laster L. 3-year longitudinal study of the periodontal status of an adult population with gingivitis. *J Clin Periodontol* 1985;12:225-38.
6. Li X, X, Kolltveit KM, Tronstad I, Olsen I. Systemic diseases caused by oral infection. *Clin Microbiol Rev* 2000;13:547-58.
7. Matilla KJ, Valtonen VV, Nieminen MS, Asikainen S. Role of infection as a risk factor for atherosclerosis, myocardial infarction, and stroke. C*lin Infect Dis* 1998;26:719-34.
8. Söder B, Yakob M, Meurman JH, Andersson LC, Klinge B, Söder PÖ. Periodontal disease may associate with breast cancer. *Breast Cancer Res Treat* 2011;127:497-502.
9. Kshirsagar A, Craig RG, Moos KL, Beck JD, Offenbacher S, Kotanko P, Klemmer PJ, Yoshino M, Levin NW, Yip JK, Almas K, Lopovici EM, Usvay LA, Falk RJ. Periodontal disease adversely affects the survival of patients with end-stage renal disease. *Kidney Int* 2009;75:746-50.
10. Taylor JJ, Preshaw PM, Lalla E. A review of the evidence for pathogenic mechanisms that may link periodontitis and diabetes. *J Clin Periodontol* 2013;40(Suppl 14):S113-34.
11. World Medical Association Declaration of Helsinki. Available from: http://www.wma.net/en/30publications/10policies/b3/17c.pdf [accessed Oct 2016].
12. Van der Weijden F, Timmerman MF, Nijboer A, Jeijerse E, Van der Velden U. Comparison of different approaches to assess bleeding on probing as indicators of gingivitis. *J Clin Periodontol* 1995;21:589-94.
13. Lobene RR, Soparkar PM, Newman MB. Use of dental floss. Effect on plaque and gingivitis. *Clin Prev Dent* 1982;4:5-8.
14. Quigley GA, Hein JW, Comparative cleansing efficiency of manual and power brushing. *J Am Dent Assoc* 1962;65:26-9.
15. Lobene RR, Weatherford T, Ross NM, Lamm RA, Menaker L. A modified gingival index for use in clinical trials. *Clin Prev Dent* 1986;8:3-6.
16. Yaacob M, Worthington H, Deacon S, Deery C, Walmsley A, Robinson P, Glenny A. Powered versus manual toothbrush for oral health. *Cochrane Database Syst Rev* 17, CD002281.
17. Holt J, Sturm D, Master A, Jenkins W, Schmitt P, Hefti A. A randomized, parallel-design study to compare the effects of the sonicare flexcare and the Oral-B P40 manual toothbrush on plaque and gingivitis. *Compend Contin Educ Dent* 2007;28:35-41.
18. Moritis K, Delaurenti M, Johnson M, Berg J, Boghosian A. Comparison of the sonicare elite and a manual toothbrush in the evaluation of plaque reduction. *Am J Dent* 2002;15(Spec Iss): 23B-5.
19. Kugel G, Boghosian A. Impact of the sonicare toothbrush on plaque and gingivitis. *Compend Contin Educ Dent* 2002;23:7-10.
20. Barlow AP, Zhou X, Roberts J, Colgan P. Effect of a novel integrated power toothbrush and toothpaste oral hygiene system on gingivitis. *Compend Contin Educ Dent* 2004;25:15-20.
21. Offenbacher S, Barros S, Mendoza L, Mauriello S, Preisser J, Moss K, de Jager M, Aspiras M. Changes in gingival crevicular fluid inflammatory mediator levels during the induction and resolution of experimental gingivitis in humans. *J Clin Periodontol* 2010;37:324-33.

The Effectiveness of Manual versus High-Frequency, High-Amplitude Sonic Powered Toothbrushes for Oral Health: A Meta-Analysis

M. de Jager, MSc, PhD A. Rmaile, BDS, MSc, PhD

Philips Research, Eindhoven, Netherlands

O. Darch, BSc (Hons), MRes, PhD

Philips Research, Cambridge, UK

J.W. Bikker, MSc, PDEng

Consultants in Quantitative Methods, Eindhoven, Netherlands

Abstract

- **Objective:** Evaluate the short-term clinical efficacy of high-frequency, high-amplitude sonic powered toothbrushes compared to manual toothbrushes on plaque removal and gingivitis reduction in everyday use through a meta-analysis of randomized controlled trials.
- **Methods:** Embase, MEDLINE, BIOSIS, Inspec, PQ SciTech, Compendex, SciSearch and IADR abstracts databases were searched. Eligible were clinical trials comparing at least one manual to one sonic powered toothbrush on plaque or gingivitis reduction over four weeks to three months in subjects without disability that could affect tooth brushing. Two authors selected and extracted data from eligible studies. When insufficient information was available, researchers were contacted. Data were pooled using random-effects models to compute standardized mean differences (SMD) and 95% confidence intervals (95% CI) quantifying differences in plaque or gingivitis reduction. Risk for bias and sources of heterogeneity were assessed.
- **Results:** The combined results of 18 studies comprising 1,870 subjects showed that sonic powered toothbrushes had statistically significantly greater plaque removal (SMD = -0.89, 95%CI = [-1.27, -0.51]) and gingivitis reduction (-0.67, [-1.01, -0.32]). Heterogeneity was large and bias was not apparent.
- **Conclusion:** High-frequency, high-amplitude sonic powered toothbrushes decreased plaque and gingivitis significantly more effectively than manual toothbrushes in everyday use in studies lasting up to three months.

(J Clin Dent 2017;28(Spec Iss A):A13–28)

Introduction

Tooth brushing is an essential means of maintaining good oral hygiene. While many individuals still rely on using manual toothbrushes, powered toothbrushing continues to increase in popularity. While manual toothbrushing can be effective, it requires skillful use and adequate duration to achieve sustained results. Powered toothbrushes have been adopted by consumers and endorsed by dental professionals as a more convenient and effective way of cleaning teeth due to a number of features, including automated bristle movement, ergonomic grips, and integrated timers to achieve the recommended two minutes of brushing.

Whether powered brushing is superior to manual brushing has been subject to controversy, as studies have demonstrated conflicting results, in part depending on such factors as study design, evaluated toothbrushes, and selected patient population. Powered toothbrushes operate with a variety of modes of action with which the bristles move, and this has been considered an important discriminator for their effectiveness.[1]

In 1992, a new type of powered toothbrush was introduced, Sonicare Advance,[2,3] with the principal and novel feature being a distinctively different mode of action compared to the then prevailing counter-rotating and oscillating-rotating principles.[4,5] This novel mode was coined a 'sonic' motion, referring to the patented high-frequency, high-amplitude, side-to-side motion of the bristles said to create a bristle tip velocity in excess of 2.0 m/s to render sufficient fluid dynamic activity for enhanced plaque removal.[6]

In effect, this sonic motion was characterized by a side-to-side bristle movement with a high frequency of over 150 Hz and a high amplitude of over 1.5 mm, with Sonicare toothbrushes typically operating at around 250 Hz and > 2 mm amplitude. This principle has been used in consecutive models of the Sonicare powered toothbrush,[3,7,8] and notably also with the Waterpik Sensonic/Sonic Speed and the Oral-B Sonic Complete.[9,10]

This rapid sonic motion was demonstrated to create a strong enough fluid dynamic effect able to dislodge and remove plaque bacteria *in vitro* up to 4 mm beyond the reach of the bristle tips in hard to reach places,[11-17] to remove plaque and reduce gingivitis more effectively than manual toothbrushes,[9,18-20] and to be safe to use on natural and restorative dental materials.[21-25]

While many individual studies have been conducted comparing the clinical efficacy of these sonic powered toothbrushes to manual and other powered toothbrushes, no comprehensive assessment of their efficacy has been reported to date, except for a well-recognized systematic review from the Cochrane collaboration.[1] This review, however, included sonic toothbrushes in the broader category of all side-to-side moving toothbrushes, including those operating with a low-amplitude and/or a low-frequency motion.[26,27] Therefore, the

objective of the study reported here was to conduct a meta-analysis of randomized controlled trials on the clinical efficacy of high-frequency, high-amplitude sonic powered toothbrushes compared to manual toothbrushes on plaque removal and gingivitis reduction in everyday use.

Materials and Methods

No review protocol was registered, yet our approach was comparable to that of the Cochrane collaboration,[1] and we have adhered to the PRISMA guidelines for reporting meta-analyses.[28]

Study Selection

This meta-analysis was constrained to randomized controlled clinical trials comparing manual with high-amplitude, high-frequency, side-to-side powered toothbrushes (further referred to as sonic toothbrushes, for brevity). All other toothbrushes operating with a low-amplitude and/or a low-frequency side-to-side motion were excluded. Included studies had to represent everyday use over a period of at least four weeks and up to three months, and report dental plaque and gingivitis outcomes. Single-use and clinician-supervised studies were excluded as these were not considered representative of everyday use. Trials were excluded if they had combined interventions (*e.g.*, brushing and flossing), but trials that allowed participants to continue with their usual oral hygiene steps, such as flossing and tongue cleaning, were included. Also included were studies with participants of any age and who had no reported impairment that might affect tooth brushing, as well as studies with participants with orthodontic appliances or with dental implants. The primary outcome measures were quantified scores of plaque or gingivitis, or both. However, plaque scores measured after participants had been instructed or permitted to brush their teeth at the assessment visit were not eligible. Where multiple gingivitis measures were reported, compound indices combining tissue color and bleeding (*e.g.*, GI, MGI) over bleeding-focused indices (*e.g.*, BOP, GBI) were used for data analysis.

Search Strategy

A combined search in seven databases comprising biomedical (Embase, MEDLINE), biology and life sciences (BIOSIS), science and technology (Inspec, PQ SciTech), and engineering (Compendex) publications, and the science citation index (SciSearch) was performed. In addition, the electronic database of abstracts from conferences of the International Association for Dental Research (IADR), as these are primary venues where investigators disseminate the results of their clinical research on toothbrushes, were also searched. This database (www.iadr.org) lists abstracts published since 2001. Two searches were performed. The broad first search looked for publications including a manual and a powered toothbrush of any kind used in a clinical study. A wide range of synonyms was used including "conventional" and "traditional" for manual toothbrushes, and "mechanic" and "rechargeable" for powered toothbrushes. The narrow second search aimed to complement the first search by selecting only additional publications with branded sonic toothbrushes, such as Sonicare or Sonic Complete, in a clinical study. Supplementary Material Number 1 summarizes the keywords used in these searches (note that all Supplementary Material cited in this article are available by request from the corresponding author). Initial searches were completed on February 16, 2016 and finally updated on August 8, 2016.

Screening and Data Extraction

Two authors (AR & OD) independently screened all titles to eliminate those clearly not comparing a manual and a powered toothbrush in a clinical study, then reviewed the remaining abstracts to exclude records that did not meet the study selection parameters described above. For the remaining records, the full paper was assessed using the same criteria, such that only eligible publications remained. They then assessed these papers independently using a common data extraction form to capture essential information. Disagreements were resolved by discussion with a third author (MdJ). Authors of eligible publications were approached when reported data were incomplete to obtain sufficiently complete records for the quantitative meta-analysis.

Data Analysis and Statistics

In these studies, outcomes for plaque or gingivitis were reported using a variety of clinical indices. To enable statistical comparisons, outcomes were converted into standardized summary measures before combining those using random-effects models. This was accomplished by calculating standardized mean differences (SMDs) and corresponding 95% Confidence Intervals (95% CI)[1] which signify the difference between the sonic and manual toothbrushes for each study individually, as well as for all studies combined. An SMD < 0 or SMD > 0 indicates a greater reduction in favor of the sonic or manual toothbrush, respectively. This reduction is considered statistically significant ($p < 0.05$) when the 95% CI excludes the zero-point. To calculate SMDs, the number of subjects (n), and the mean and standard deviation (SD) of plaque and gingivitis outcomes at the final visit for both study groups were needed. When a standard error (SE) was reported, it was simply converted to SD using SD=SE*SQRT(n); when median and interquartile ranges were provided, these were recalculated following Luo, *et al.*[29] and Wan, *et al.*[30]

Risk of bias across studies was assessed by inspecting the symmetry of a "funnel plot" depicting the SE versus the SMD of all studies. Additionally, heterogeneity of study outcomes was evaluated, and subgroup and sensitivity analyses were performed to assess the effect of variations in study characteristics on outcomes and heterogeneity.

The meta-analysis and generation of forest and funnel plots were performed with the Stata software module *metan*.[31,32]

Results

Both Figure 1 and Supplementary Material Number 2 summarize the study selection for both searches. The combined search in seven publication databases provided 450 titles. After screening the titles for relevance, *i.e.*, suggestive of comparing toothbrushes on plaque or gingivitis in a clinical study, 214 abstracts remained of which only 30 were retained as possibly eligible for inclusion in the meta-analysis after review. Full paper review excluded another 15 papers, leaving 15 eligible papers. Of these 15 papers, three were excluded from the quantitative analysis; one because data were incomplete and the authors could no longer provide required data,[33] another because the powered toothbrush model was not specified and the authors did not respond to our request for information,[34] and a final study was not

included since it only provided data at 12 months.[35] Thus, from this search, 12 studies could be included in the meta-analysis.[18,20,36–45]

The search in the IADR database of conference abstracts yielded 651 records, 13 of which were retained as eligible after successive screening steps. None of these studies were published as full papers. After reviewing these 13 abstracts, five were excluded since the authors did not respond to our inquiries for additional information: two abstracts about the same study on patients with implants did not report usable plaque or gingivitis data,[46,47] another two abstracts reported incomplete data,[48,49] and the fifth abstract did not specify the type of powered toothbrush used in the study.[50] Eventually, eight eligible abstracts remained with sufficient data to include in the meta-analysis.[51–58]

In summary, of 1,101 records retrieved, 20 studies qualified and provided sufficient data for inclusion in the meta-analysis to specifically compare the efficacy of sonic powered toothbrushes against manual toothbrushes on plaque removal or gingivitis reduction over a period of four weeks to three months. Table I lists these studies. Most studies included adults, three studies had adolescents with orthodontic brackets, and a further three studies selected subjects to evaluate plaque and gingivitis reduction around implants, of which only one study reported data for natural teeth separately. Therefore, rather than

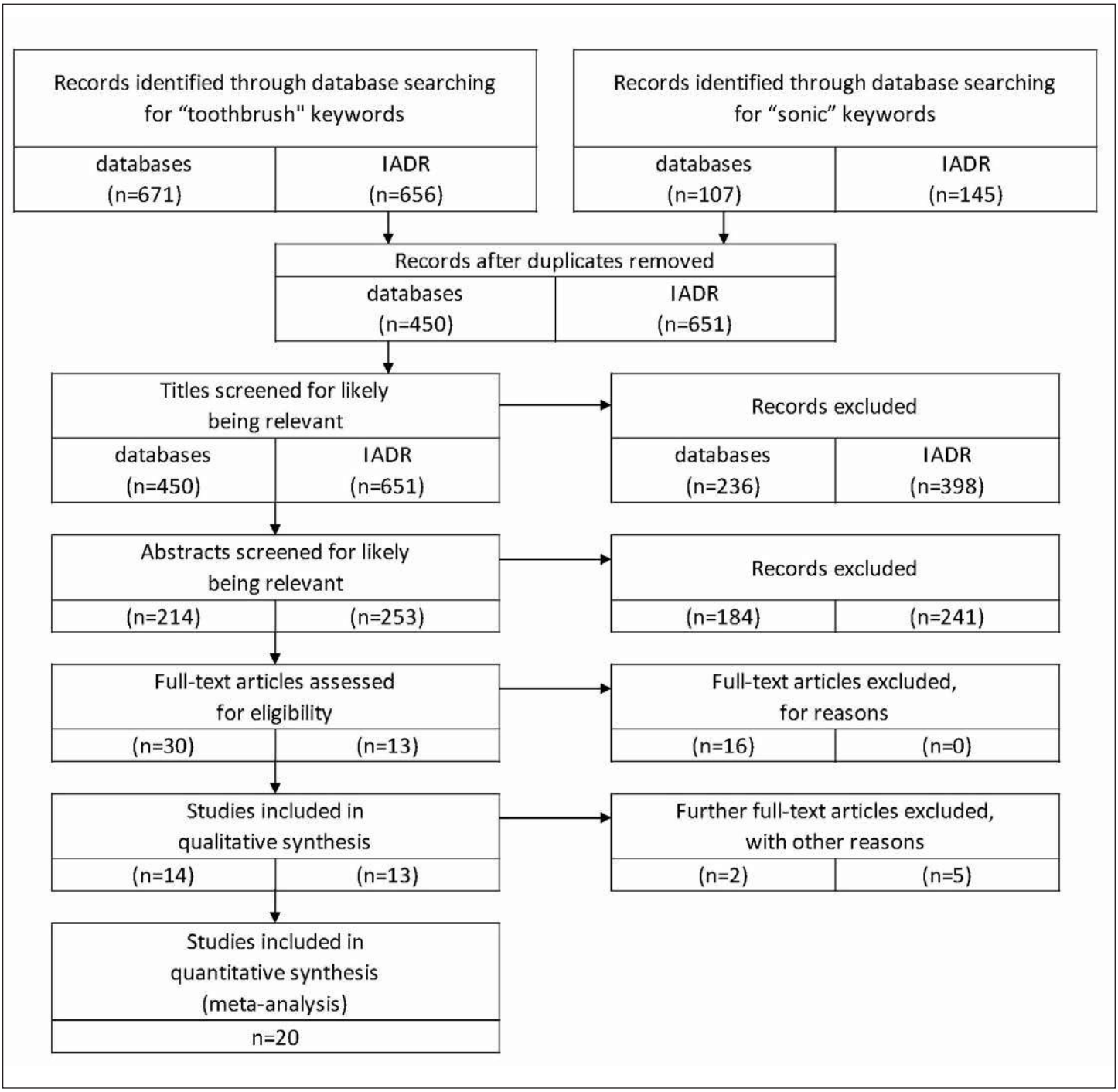

Figure 1. *Study selection flow chart.*

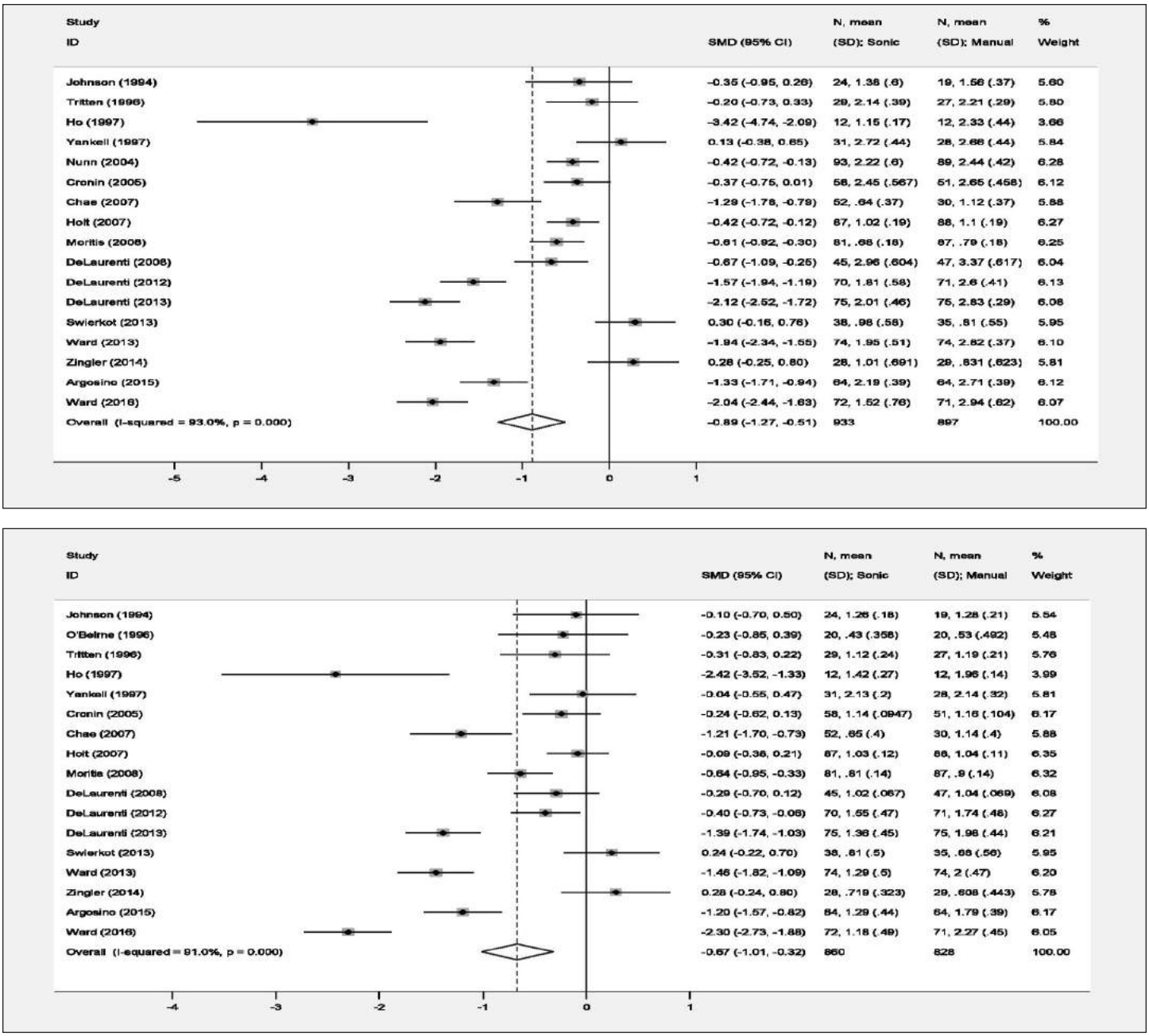

Figure 2. *Results and forest plots for each study with Standardized Mean Difference (SMD) and 95% Confidence Intervals (95%CI) comparing sonic powered versus manual toothbrushes for (top) plaque removal and (bottom) gingivitis reduction. SMD<0 favors the powered toothbrush. 'N' refers to number of subjects, 'mean' is the mean plaque or gingivitis score, and 'SD' the corresponding standard deviation. 'Weight' is the respective weight attributed to each study in the overall assessment using random-effects model.*

excluding these implant studies for not being generalizable, we analyzed them separately for comparative efficacy around implants. Publication dates ranged from 1994 through 2016. Key data extracted for the meta-analysis included the number of subjects for each toothbrush group with the corresponding plaque or gingivitis scores (mean and standard deviation), and study duration. Annex 1 summarizes each included study in detail.

Overall, 18 studies with a total of 1,870 subjects were combined, of which one study reported only data on plaque removal and another only on gingivitis reduction, thus yielding 17 studies for both comparisons. Figure 2 (left panel) demonstrates that sonic powered toothbrushes yielded a significantly greater amount of plaque reduction compared to manual toothbrushes, reporting an SMD = -0.89 and 95% CI = [-1.27, -0.51]. Similarly, Figure 2 (right panel) shows a significantly larger reduction in gingivitis scores for sonic toothbrushes relative to manual ones, with SMD = -0.67 and 95% CI = [-1.01, -0.32].

Study heterogeneity was large in both analyses at 93% and 91%, respectively. Funnel plots, shown in Figure 3, depict the SMD and its SE for the individual studies as a means to visualize possible bias in (smaller) studies when there is asymmetry in the results. Overall, bias does not appear to be present, despite one smaller study on 24 orthodontic adolescents being included[38] (displayed in the lower left-hand corner of the graphs). To examine the influence on overall outcomes of this study and other studies, sensitivity was investigated by excluding this study, the one study focused on Sonic Complete,[51] and all "non-typical" studies, that is, those which included orthodontic or implant

subjects,[36,38,42,53] reported incomplete data[39,45] or used a three-minute brushing period.[58] Excluding these studies, however, did not appreciably reduce heterogeneity or affect the overall outcomes (Table II). Additionally, subgroup analyses were performed with one group including the obsoleted initial 'Sonicare Advance' models (five studies) and the other group including more recent Sonicare models (12 studies; Table II). In the first group, SMDs and heterogeneity were reduced, but a larger 95% CI resulted to the effect that no significant differences over manual toothbrushes could be detected. In contrast, for the second group, outcomes relative to manual toothbrushes improved somewhat.

For data on efficacy around implants, three studies with 149 subjects were analyzed separately.[36,41,43] Results show that while sonic toothbrushes appeared to perform better on average, no statistically significant differences were obtained when comparing the efficacy between sonic and manual toothbrushes in removing plaque (SMD = -0.36, 95% CI = [-1.02, 0.30]) or reducing gingival inflammation (SMD = -0.32, 95% CI = [-0.76, 0.12]) around implants (see Supplementary material 3).

Discussion

Overall, this meta-analysis demonstrated a greater ability for sonic powered toothbrushes to remove plaque and reduce gingivitis compared to manual toothbrushes in everyday use in studies ranging from four weeks to three months duration. Studies were selected via an extensive database search of published papers, as well as a focused search in the electronic database of abstracts from IADR conferences. Our results confirm the validity of this approach since the IADR search revealed an additional 13 eligible studies which were not published as formal papers, of which eight could be included in the meta-analysis. Where necessary, authors of papers and abstracts were contacted with a request for complementary data.

Strengths of our approach include: the comprehensive literature search which included data from studies not published as full papers but retrieved initially as IADR abstracts; the focus on a singular (*i.e.*, high-frequency, high-amplitude sonic) mode of action of powered toothbrushes; and the relatively large pool of included studies, including nearly 1,900 adult and adolescent subjects with a variety of oral conditions (gingivitis, periodontitis, implants, and orthodontic appliances), thus making the outcomes generalizable to normal use in an everyday population across the spectrum of oral health and disease.

Limitations may include the following. First, the short-term focus (up to three months) due to a paucity of longer-term studies with sonic toothbrushes. We found only four long-term studies, of which two also reported three-month data that were included in our assessment.[36,43] One six-month study concluded in favor of sonic toothbrushes in patients with dental implants,[43] two 12-month studies revealed no significant differences between the evaluated toothbrushes in patients with gingival recession or dental implants, respectively,[35,36] and a further study on implant patients reported outcomes in favor of sonic toothbrushes up to a period of 48 months.[46,47] Overall, this suggests further long-term studies are required in representative populations.

Second, the exclusion of three out of 23 eligible short-term studies due to lack of reported data and inability to obtain further information might have introduced selection bias. This appears unlikely, since two studies concluded in favor of Sonicare Elite[48] and Waterpik Sensonic,[49] respectively, and one study found no significant difference for the Waterpik Sonic Speed.[33]

A third limitation may be the large heterogeneity among the studies. This, however, is not uncommon in meta-analyses and, possibly, is even unavoidable due to the inherent variety associated with these

Table I
Key Characteristics of Included Studies

Nr.	Reference	Subjects	Powered Toothbrush	Manual Toothbrush	Plaque Index	Gingival Index	Final Timepoint
1	Johnson 1994	Adults with gingivitis, 20-54 yrs	Sonicare Advance	Oral-B 30	TQH	A&B	4 weeks
2	O'Beirne 1996	Adults with periodontitis, 18-65 yrs	Sonicare Advance	Oral-B	n/a	L&S	8 weeks
3	Tritten 1996	Adults with gingivitis, 18-65 yrs	Sonicare Advance	Butler 311	TQH	L&S	12 weeks
4	Ho 1997	Orthodontic adolescents, 11-18 yrs	Sonicare Advance	Oral-B P 35	S&L	L&S	4 weeks
5	Yankell 1997	Adults, 18-50 yrs	Sonicare Advance	Oral-B P 35	TQH	L&S	30 days
6	Nunn 2004	Adults, 18-68 yrs	Sonicare Crest IntelliClean	Oral-B P 35	TQH	n/a	4 weeks
7	Cronin 2005	Not specified	Oral-B Sonic Complete	not provided	TQH	L&S	3 months
8	Chae 2007	Adults with mild-moderate periodontitis, 25-55 yrs	Sonicare Elite	Butler 311	S&L	L&S	12 weeks
9	Holt 2007	Adults with moderate gingivitis, 18-64 yrs	Sonicare FlexCare	Oral-B P40	S&L	L&S	4 weeks
10	Moritis 2008	Adults with moderate gingivitis, 19-62 yrs	Sonicare Elite	Oral-B P40	S&L	L&S	4 weeks
11	DeLaurenti 2008	Orthodontic subjects, 12-42 yrs	Sonicare FlexCare	Oral-B P40	TQH	L&S	4 weeks
12	DeLaurenti 2012	Adults with mild-moderate gingivitis, 20-70 yrs	Sonicare FlexCare+	ADA reference	TQH	MGI	4 weeks
13	DeLaurenti 2013	Adults with mild-moderate gingivitis, 18-64 yrs	Sonicare FlexCare Platinum	ADA reference	TQH	MGI	4 weeks
14	Swierkot 2013*	Partially edentulous with posterior implants, 45-78 yrs	Sonicare FlexCare	Oral-B P40	S&L	L&S	3 months
15	Ward 2013	Adults with mild-moderate gingivitis, 18-65 yrs	Sonicare FlexCare Platinum	ADA reference	TQH	MGI	4 weeks
16	Zingler 2014	Orthodontic adolescents, 11-15 yrs	Sonicare FlexCare	Elmex	TQH	PBI	12 weeks
17	Argosino 2015	Adults with mild-moderate gingivitis, 18-64 yrs	Sonicare 3-series	ADA reference	TQH	MGI	4 weeks
18	Ward 2016	Adults with mild-moderate gingivitis, 19-64 yrs	Sonicare FlexCare Platinum	ADA reference	TQH	MGI	6 weeks
	Implant studies						
14	Swierkot 2013*	Partially edentulous with posterior implants, 45-78 yrs	Sonicare FlexCare	Oral-B P40	S&L	L&S	3 months
19	Wolff 1998	Adults with implant restorations, 21-73 yrs	Sonicare Advance	Crest Complete	S&L	L&S	12 weeks
20	Lee 2015	Implant patients with peri-implant mucositis, 27-75 yrs	Sonicare DiamondClean	Butler GUM 311	mPI	mSBI	2 months

TQH = Turesky-modified Quigley & Hein plaque index, S&L = Silness & Löe plaque index, mPI = modified plaque index, A&B = Ainamo and Bay gingival index, L&S = Löe & Silness gingival index, MGI = modified gingival index, PBI = papillary bleeding index, mSBI = modified sulcus bleeding index. (*Study reported data for natural teeth and implant sites separately.)

types of clinical studies. This variety may be due to the diversity of designs of powered and manual toothbrushes and their continued evolution over time, and variations in study designs, in particular the choice of clinical indices, subject characteristics, and study duration. Our sensitivity and subgroup analysis did not yield further insights into possible causes for heterogeneity in this meta-analysis. Nevertheless, to reduce heterogeneity, greater uniformity in study design may be achieved in following the recommendations of Robinson, *et al.*[59]

Our approach was comparable to the one advocated by the Cochrane collaboration in their systematic reviews of powered toothbrushes.[1,60] Our approach differed in that we focused specifically on high-frequency high-amplitude sonic powered toothbrushes, as a relevant and distinctive subset of the more generic side-to-side category recognized by the Cochrane collaboration. It is therefore interesting to compare our outcomes specifically with the most recent Cochrane results[1] on side-to-side, as well as oscillating-rotating toothbrushes, the latter being the other prevailing mode of action in powered toothbrushes to date. Table III and Supplementary Material 4 show this comparison and illustrate that sonic-only, as well as oscillating-rotating, but not side-to-side toothbrushes, achieved significantly greater reductions over manual toothbrushes. Another relevant assessment can be made now in statistically comparing sonic versus oscillating-rotating toothbrushes using manual toothbrush as the generic control. It followed that results were suggestive of a favorable effect for sonic over oscillating-rotating toothbrushes for plaque removal ($p = 0.10$) and comparable for gingivitis reduction ($p = 0.41$; Annex 2). This result indicates that both modes of operation confer a comparable

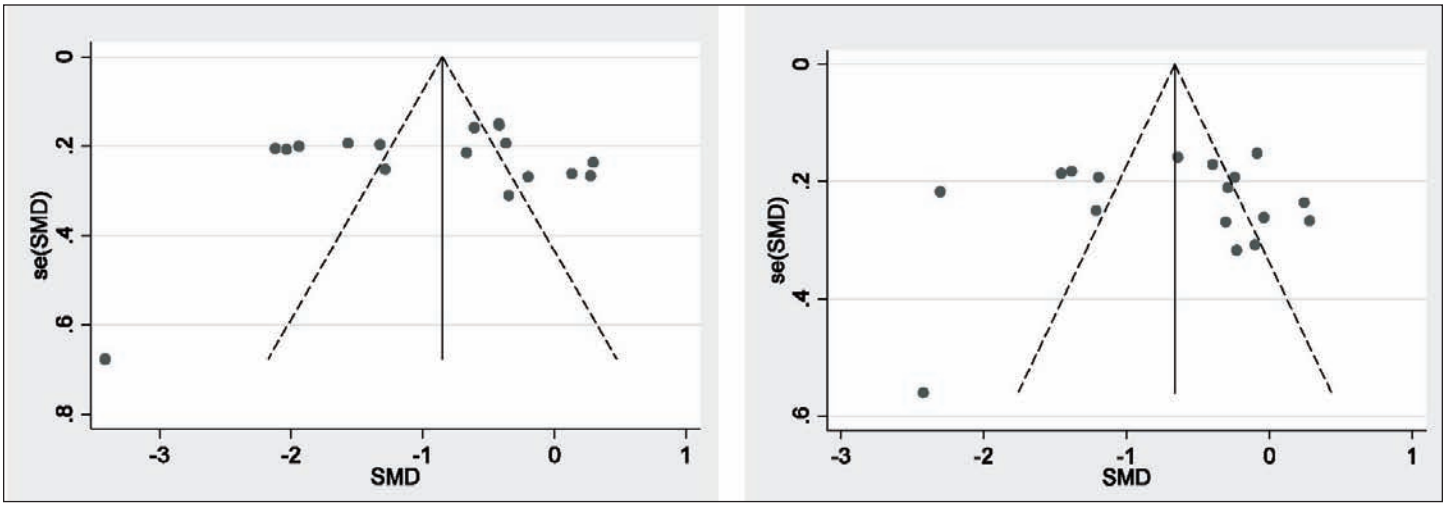

Figure 3. *Funnel plots for (left) plaque and (right) gingivitis outcomes showing SMD and standard error (se) of SMD with 95% pseudo confidence intervals to identify apparent study outliers through assymetry in results.*

Table II
Sensitivity and Subgroup Analysis with Effect on Outcomes and Heterogeneity (I^2)

		Plaque Removal					Gingivitis Reduction				
	Studies*	n	SMD	95%CI	p-value	I^2	n	SMD	95%CI	p-value	I^2
Overall analysis		1830	-0.89	[-1.27, -0.51]	< 0.0001	93.0%	1688	-0.67	[-1.01, -0.32]	< 0.001	91.0%
Sensitivity Analyses	Excluded										
Apparent outlier	4	1806	-0.80	[-1.18, -0.42]	< 0.0001	93.0%	1664	-0.60	[-0.94, -0.25]	< 0.001	91.1%
Non-Sonicare study	7	1721	-0.93	[-1.33, -0.52]	< 0.0001	93.2%	1579	-0.70	[-1.06, -0.33]	< 0.001	91.4%
All non-typical studies	2,4,6,11,14,16,18	1259	-0.92	[-1.36, -0.49]	< 0.0001	92.2%	1259	-0.65	[-0.98, -0.32]	< 0.001	87.4%
Subgroup Analyses	Included										
Only Sonicare Advance	1-5	182	-0.74	[-1.67, 0.18]	0.12	87.6%	222	-0.47	[-1.03, 0.09]	0.10	74.8%
Only later Sonicare models	6, 8-18	1539	-0.99	[-1.43, -0.54]	< 0.0001	93.9%	1357	-0.77	[-1.21, -0.33]	< 0.001	93.3%

*Study numbers refer to Table I.

Table III
Comparing Outcomes of This Study with Results for Other Modalities as Reported by Yaacob, et al.[1]

Modality	Nr of Studies	Nr of Subjects	SMD	95%CI	p-value	I^2	Source
Plaque Removal							
Sonic	17	1830	-0.89	[-1.27, -0.51]	p < 0.001	93%	This paper
Side-to-side	7	570	-0.27	[-0.77, 0.23]	p = 0.29	87%	Cochrane analysis 2.1
Rotating-oscillating	20	1404	-0.53	[-0.74, -0.31]	p < 0.001	72%	Cochrane analysis 4.1
Gingivitis Reduction							
Sonic	17	1688	-0.67	[-1.01, -0.32]	p < 0.001	91%	This paper
Side-to-side	9	795	-0.32	[-0.81, 0.17]	p = 0.20	90%	Cochrane analysis 2.2
Rotating-oscillating	21	1479	-0.49	[-0.73, -0.26]	p < 0.001	78%	Cochrane analysis 4.2

clinical advantage over manual toothbrushing. This corroborates the general conclusion from the Cochrane report that "powered toothbrushes reduce plaque and gingivitis more than manual tooth brushing in the short and long term,"[1] yet seemingly contradicts another Cochrane review that compared powered toothbrushes[60] and concluded "that rotation-oscillation brushes reduce plaque and gingivitis more than side-to-side brushes in the short term." By focusing on sonic brushing as a separate mode of action, our analysis demonstrated that this conclusion does not apply to side-to-side toothbrushes using a high-amplitude, high-frequency bristle motion.

A useful method to interpret SMDs in terms of plaque and gingivitis reduction is to refer to studies with a comparable SMD/CI.[1] For plaque reduction (SMD = -0.89), the nearest larger studies with a representative population would be either Moritis, *et al.*,[37] albeit with a slight underestimate (SMD = -0.61) or Argosino, *et al.*,[56] with a slight overestimate (SMD = -1.33), which reported that the manual toothbrush had, respectively, 16% and 24% more plaque remaining at the final time point of evaluation. Concurrently, for gingivitis reduction (SMD = -0.67), the results are comparable to Moritis, *et al.*[37] (SMD = -0.64), which showed that manual toothbrushes had 11% higher gingivitis levels at study conclusion. Therefore, this analysis indicates that sonic tooth brushing yielded about 10% to 20% greater improvements in clinical outcomes indicative for oral health.

In conclusion, this meta-analysis of 18 short-term studies, encompassing nearly 1,900 subjects, demonstrated a significantly greater ability of high-frequency, high-amplitude sonic powered toothbrushes to remove plaque and reduce gingivitis in everyday use in an everyday population when compared to manual toothbrushes. This provides clinicians with sound evidence on which to base their recommendations to patients.

Acknowledgments: The authors kindly thank Drs. C. Kossack and P.G. Jost-Brinkmann, Drs. J. Lee and S. Kim, Dr. S. Zingler and colleagues, and Dr. M. Ward for responding to our requests and providing more information. We also thank Mr. J. Dielis of the Center for Information Services of Philips Research for help with the literature search, as well as Ms. W. Jenkins, Mr. W. Staerker, Dr. M. Yakob, and Dr. M. Watts for their suggestions in preparing the manuscript.

Conflict of Interest: MJ, AR, and OD are employees of Philips, maker of the Sonicare sonic powered toothbrush, which is included in the scope of this meta-analysis. JWB is an independent statistician with Consultants in Quantitative Methods, commissioned by Philips for contributions to this work.

Supplementary Materials: Supplementary materials may be obtained from the corresponding author of this paper upon request.

For correspondence with the authors of this paper, contact Dr. M. de Jager –marko.de.jager@philips.com.

References

1. Yaacob M, Worthington HV, Deacon SA, Deery C, Walmsley AD, Robinson PG, Glenny AM. Powered versus manual toothbrushing for oral health (Review). *Cochrane Database Syst Rev* 2014;17:CD002281.
2. Emling RC, Yankell SL. The application of sonic technology to oral hygiene: the third generation of powered toothbrushes. *J Clin Dent* 1997;8(Spec Iss 1):1-3.
3. McInnes C, Pace JW. Designing the next generation of a sonic toothbrush. *Am J Dent* 2002;15(Spec Iss):4B-6.
4. Khocht A, Spindel L, Person P. A comparative clinical study of the safety and efficacy of three toothbrushes. *J Periodontol* 1992;63:603-10.
5. Barnes CM, Weatherford TW, Menaker L. A comparison of the Braun Oral-B Plaque Remover (D5) electric and a manual toothbrush in affecting gingivitis. *J Clin Dent* 1993;4:48-51.
6. Giuliani D, Martin RW. United States Patent 5,378,153. 1992.
7. Dudgeon DJ, Barlow AP. A novel oral hygiene system through integration of a sonic toothbrush and liquid toothpaste. *Compend Contin Educ Dent* 2004;25 (Suppl 1):4-7.
8. Black C, Hall S, Headstrom P, Kloster T, Kotlarchik G, Kulas A, Lumbantobing A, Miller K, Wills S. A new generation of Sonicare power toothbrushes – The FlexCare series. *Compend Contin Educ Dent* 2007;28(Suppl 1):4-9.
9. Zimmer S, Fosca M, Roulet JF. Clinical study of the effectiveness of two sonic toothbrushes. *J Clin Dent* 2000;11:24-7.
10. Versteeg PA, Timmerman MF, Rosema NAM, Warren PR, Van der Velden U, Van der Weijden GA. Sonic-powered toothbrushes and reversal of experimental gingivitis. *J Clin Periodontol* 2005;32:1236-41.
11. McInnes C, Engel D, Martin RW. Fimbria damage and removal of adherent bacteria after exposure to acoustic energy. *Oral Microbiol Immunol* 1993;8:277-82.
12. Stanford CM, Srikantha R, Wu CD. Efficacy of the Sonicare toothbrush fluid dynamic action on removal of human supragingival plaque. *J Clin Dent* 1997;8(Spec Iss 1):10-4.
13. Hope CK, Wilson M. Comparison of the interproximal plaque removal efficacy of two powered toothbrushes using *in vitro* oral biofilms. *Am J Dent* 2002;15(Spec Iss):7B-11.
14. Adams H, Winston MT, Heersink J, Buckingham-Meyer KA, Costerton JW, Stoodley P. Development of a laboratory model to assess the removal of biofilm from interproximal spaces by powered tooth brushing. *Am J Dent* 2002;15(Spec Iss):12B-17.
15. Aspiras M, Elliott N, Nelson R, Hix J, Johnson M, De Jager M. *In vitro* evaluation of interproximal biofilm removal with power toothbrushes. *Compend Contin Educ Dent* 2007;28(Suppl. 1):10-4.
16. Blanco VL, Cobb CM, Williams KB, Manch-Citron JN. *In vitro* effect of the Sensonic toothbrush on Treponema denticola. *J Clin Periodontol* 1997;24:318-23.
17. MacNeill S, Walters DM, Dey A, Glaros AG, Cobb CM. Sonic and mechanical toothbrushes. An *in vitro* study showing altered microbial surface structures but lack of effect on viability. *J Clin Periodontol* 1998;25:988-93.
18. Tritten CB, Armitage GC. Comparison of a sonic and a manual toothbrush for efficacy in supragingival plaque removal and reduction of gingivitis. *J Clin Periodontol* 1996;23:641-48.
19. Moritis K, Delaurenti M, Johnson MR, Berg J, Boghosian AA. Comparison of the Sonicare Elite and a manual toothbrush in the evaluation of plaque reduction. *Am J Dent* 2002;15(Spec Iss):23B-25.
20. Holt J, Sturm D, Master A, Jenkins W, Schmitt P, Hefti AF. A randomized, parallel-design study to compare the effects of the Sonicare FlexCare and the Oral-B P40 manual toothbrush on plaque and gingivitis. *Compend Contin Educ Dent* 2007;28(Suppl 1):35-41.
21. Donly KJ, Vargas M, Meckes M, Sharma A, Kugel G, Hurley E. *In vitro* comparison of restoration wear and tensile strength following extended brushing with Sonicare and a manual toothbrush. *J Clin Dent* 1997;8(Spec Iss):30-5.
22. Sorensen JA, Nguyen HK. Evaluation of toothbrush-induced dentin substrate wear using an *in vitro* ridged-configuration model. *Am J Dent* 2002;15(Spec Iss):26B-32B.
23. de Jager M, Nelson R, Schmitt P, Moore M, Putt M, Kunzelmann K-H, Nyamaa I, Garcia-Godoy F, Garcia-Godoy C. *In vitro* assessment of toothbrush wear on natural and restorative materials. *Compend Contin Educ Dent* 2007;28(Suppl 1):42-50.
24. García-Godoy F, de Jager M. Effect of manual and powered toothbrushes on orthodontic bracket bond strength. *Am J Dent* 2007;20:90-2.
25. Hansen PA, Woolsey G, Killoy WJ, Hanson C. Effect of brushing with sonic and counterrotational toothbrushes on the bond strength of full veneer crowns. *J Prosthet Dent* 1998;80:429-33.
26. Sharma NC, Qaqish JG, He T, Walters PA, Grender JM, Biesbrock AR. Plaque and gingivitis reduction efficacy of an advanced pulsonic toothbrush: a 4-week randomized and controlled clinical trial. *Am J Dent* 2010;23:305-10.
27. Walsh M, Heckman B, Leggott P, Armitage G, Robertson PB. Comparison of manual and power toothbrushing, with and without adjunctive oral irrigation, for controlling plaque and gingivitis. *J Clin Periodontol* 1989;16:419-27.
28. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097.
29. Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range and/or mid-quartile range. *eprint arXiv:150505687* 2015;http://arxiv.org/abs/1505.05687 [last accessed 26 July 2016]
30. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol* 2014;14:135.
31. Harris RJ, Bradburn MJ, Deeks JJ, Altman DG, Harbord RM, Sterne JAC. Metan: Fixed- and random-effects meta-analysis. *Stata J* 2008;8:3-28.
32. Harris R, Bradburn M, Deeks J, Altman D, Harbord R, Steichen T, Sterne J.

METAN: Stata module for fixed and random effects meta-analysis. 2006;https://ideas.repec.org/c/boc/bocode/s456798.html [last accessed 22 July 2016]
33. Kossack C, Jost-Brinkmann P-G. Plaque and gingivitis reduction in patients undergoing orthodontic treatment with fixed appliances-comparison of toothbrushes and interdental cleaning aids. A 6-month clinical single-blind trial. *J Orofac Orthop* 2005;66:20-38.
34. Kallar S, Pandit IK, Srivastava N, Gugnani N. Plaque removal efficacy of powered and manual toothbrushes under supervised and unsupervised conditions: a comparative clinical study. *J Indian Soc Pedod Prev Dent* 2011;29:235-58.
35. McCracken GI, Heasman L, Stacey F, Swan M, Steen N, De Jager M, Heasman PA. The impact of powered and manual toothbrushing on incipient gingival recession. *J Clin Periodontol* 2009;36:950-7.
36. Swierkot K, Brusius M, Leismann D, Nonnenmacher C, Nüsing R, Lubbe D, Schade-Brittinger C, Mengel Rl. Manual versus sonic-powered toothbrushing for plaque reduction in patients with dental implants: an explanatory randomised controlled trial. *Eur J Oral Implantol* 2013;6:133-44.
37. Moritis K, Jenkins W, Hefti A, Schmitt P, McGrady M. A randomized, parallel design study to evaluate the effects of a Sonicare and a manual toothbrush on plaque and gingivitis. *J Clin Dent* 2008;19:64-8.
38. Ho HP, Niederman R. Effectiveness of the Sonicare sonic toothbrush on reduction of plaque, gingivitis, probing pocket depth and subgingival bacteria in adolescent orthodontic patients. *J Clin Dent* 1997;8:15-9.
39. O'Beirne G, Johnson RH, Persson GR, Spektor MD. Efficacy of a sonic toothbrush on inflammation and probing depth in adult periodontitis. *J Periodontol* 1996;67:900-8.
40. Johnson BD, McInnes C. Clinical evaluation of the efficacy and safety of a new sonic toothbrush. *J Periodontol* 1994;65:692-7.
41. Lee J, Lim J Heun, Lee J, Kim S, Koo KT, Seol YJ, Ku Y, Lee YM, Rhyu IC. Efficacy of sonic-powered toothbrushes for plaque removal in patients with peri-implant mucositis. *J Periodontal Implant Sci* 2015;45:56-61.
42. Zingler S, Pritsch M, Wrede DJ, Ludwig B, Bister D, Kneist S, Lux CJ. A randomized clinical trial comparing the impact of different oral hygiene protocols and sealant applications on plaque, gingival, and caries index scores. *Eur J Orthod* 2014;36:150-63.
43. Wolff L, Kim A, Nunn M, Bakdash B, Hinrichs J. Effectiveness of a sonic toothbrush in maintenance of dental implants. A prospective study. *J Clin Periodontol* 1998;25:821-8.
44. Yankell SL, Emling RC. A thirty-day safety and efficacy evaluation of the Rowenta, Braun and Sonicare powered toothbrushes and a manual toothbrush. *J Clin Dent* 1997;8:120-7.
45. Nunn ME, Ruhlman CD, Mallatt PR, Rodriguez SM, Ortblad KM. Plaque reduction over time of an integrated oral hygiene system. *Compend Contin Educ Dent* 2004;25:8-14.
46. Juric R, Simoncic B, Sotošek B, Kansky A, Seme K. Sonic vs. manual toothbrush: The effect on periimplant tissues and microflora. *J Dent Res* 2002;81(Spec Iss A):0611 (www.iadr.org).
47. Juric R, Simoncic B, Seme K, Kansky A, Sotošek B. Longterm effect of sonic toothbrush on periimplant tissues and microbiota. *J Dent Res* 2004;83(Spec Iss A):0836 (www.iadr.org).
48. Clausnitzer CE, Termaat SHM, Kruse AE, Hellmich M, Noack MJ. The efficacy of a sonic electric toothbrush in periodontal patients. *J Dent Res* 2005;84(Spec Iss A):0100 (www.iadr.org).
49. Roggendorf HC, Rüther B, Stark H. Oral hygiene by utilization of different dental brushes in elderly. *J Dent Res* 2005;87(Spec Iss B):1116 (www.iadr.org).
50. Lin H-C, Cui TG, Zhi QH, Zhou Y. Plaque control effectiveness of electric toothbrush in visually impaired students. *J Dent Res* 2013;92(Spec Iss C):0095 (www.iadr.org).
51. Cronin MJ, Dembling WZ, Cugini MA, Thompson MC, Warren PR. 3-Month assessment of safety and efficacy of two toothbrushes. *J Dent Res* 2005;84(Spec Iss A):0933 (www.iadr.org).
52. Chae GJJ, Hong JYY, Yoo HSS, Jung SWW, Choi SHH, Kim CKK, Sturm D. Effects of Sonicare toothbrush in slight to moderate chronic periodontitis. *J Dent Res* 2007;86(Spec Iss A):1066 (www.iadr.org).
53. DeLaurenti M, Putt MS, Milleman JL, Jenkins W, Wei J, Strate J. Plaque removal by Sonicare and manual toothbrushes in orthodontic subjects. *J Dent Res* 2008;87(Spec Iss B):2044 (www.iadr.org).
54. DeLaurenti M, Putt MS, Milleman JL, Milleman K, Ward M, Jenkins W, Souza S, Nelson M. An evaluation of two toothbrushes on plaque and gingivitis. *J Dent Res* 2012;91(Spec Iss B):0522 (www.iadr.org).
55. DeLaurenti M, Souza S, Nelson M, Jenkins W, Argosino K, Ward M, Milleman J, Milleman KR. Investigation of a novel sonic toothbrush on plaque and ingivitis. *J Dent Res* 2013;92(Spec Iss A):3748 (www.iadr.org).
56. Argosino K, Milleman J, Milleman K, Mwatha A, Ward M, Jenkins W, Souza S. An evaluation of power toothbrushing on gingivitis and plaque biofilm. *J Dent Res* 2015;94(Spec Iss A):3075 (www.iadr.org).
57. Ward M, Jenkins W, Argosino K, Souza S, Nelson M, Milleman J, Milleman KR. Assessment of a sonic toothbrush on plaque and gingivitis. *J Dent Res* 2013;92(Spec Iss A):3753 (www.iadr.org).
58. Ward M, Yu X, Souza S, Jenkins W, Milleman J, Milleman K, Dafenbaugh J. Assessment of AdaptiveClean brush head on plaque and gingivitis. *J Dent Res* 2016;95(Spec Iss A):0460 (www.iadr.org).
59. Robinson PG, Damien Walmsley A, Heanue M, Deacon S, Deery C, Glenny AM, Worthington H, Shaw W. Quality of trials in a systematic review of powered toothbrushes: suggestions for future clinical trials. *J Periodontol* 2006;77:1944-53.
60. Deacon SA, Glenny A-M, Deery C, Robinson PG, Heanue M, Walmsley AD, Shaw WC. Different powered toothbrushes for plaque control and gingival health. *Cochrane Database Syst Rev*. 2010;12:CD004971.

Annex 1
Details of Included Studies (in Chronological Order)

Study	**Johnson 1994**
Design	RCT, parallel, single blind, 4 weeks, 53 subjects with 2 drop outs and 8 with missed visits.
Participants	USA, adult, ≥ 20 teeth, Löe and Silness gingival index ≥ 1.5 on Ramfjord teeth, no medical conditions, 20 to 54 years (18M, 33F).
Interventions	Sonicare Advance versus Oral-B 30, 2 minutes twice daily. Instructions. Timer supplied.
Outcome measures	Turesky-modified Quigley and Hein plaque index on all sites, Ainamo and Bay gingival index (A&B) and sulcular bleeding index on Ramfjord teeth at baseline, 1, 2, 4 weeks. Soft tissue trauma "abnormalities" 7 sites in 6 subjects for manual and 10 sites in 7 subjects for powered.
Notes	Manufacturer funded. Data from post-brushing evaluation used in analysis.

Results	**Plaque Index**						**Gingival Index (A&B)**					
	Baseline			Week 4			Baseline			Week 4		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Advance	24	1.86	0.54	24	1.38	0.60	24	1.47	0.17	24	1.26	0.18
Oral-B 30	19	1.71	0.50	19	1.56	0.37	19	1.58	0.16	19	1.28	0.21

Study	O'Beirne 1996
Design	RCT, parallel, single blind, 8 weeks, 40 subjects, drop outs unclear.
Participants	USA, adults with periodontal inflammation, ≥ 20 teeth and received periodontal treatment (but not within 30 days of participation), 32 to 64 years (22M, 18F).
Interventions	Sonicare Advance versus Oral B manual, 2 minutes twice daily. Instructions. Timer supplied.
Outcome measures	Löe and Silness gingival index (L&S), Barnett papillary bleeding index at baseline, 2, 4, 8 weeks, at three test sites (with PD 5-7 mm). Whole mouth recording PD. Minor gingival trauma seen in one participant in each group.
Notes	Partly funded by manufacturer.

Results	Plaque Index	Gingival Index (L&S)					
		Baseline			Week 8		
	n.a.	n	Mean	SD	n	Mean	SD
Sonicare Advance		20	1.80	0.27	20	0.43	0.36
Oral-B		20	1.75	0.45	20	0.53	0.49

Study	Tritten 1996
Design	RCT, parallel, single blind, 12 weeks, 60 subjects with 4 drop outs.
Participants	USA, adults 22 to 59 years (32M, 28F), GI >1.5 (on Ramfjord teeth), no PD>5mm, dental hospital patients, no professional cleaning previous 3 months, minimum 20 teeth, no previous periodontal treatment and not pregnant.
Interventions	Sonicare Advance versus Butler #311, 2 minutes twice daily. Instructions. Timer supplied.
Outcome measures	Turesky-modified Quigley and Hein plaque index all teeth; Löe and Silness gingival index and bleeding on probing on Ramfjord teeth; recorded at baseline, 1, 2, 4, 12 weeks. Gingival abrasion seen in five manual and one powered brush subjects.
Notes	Manufacturer funded. Abstain from oral hygiene 12-14h for pre-brushing evaluations.

Results	Plaque Index						Gingival Index					
	Baseline			Week 12			Baseline			Week 12		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Advance	29	2.70	0.57	29	2.14	0.39	29	1.40	0.10	29	1.12	0.24
Butler 311	27	2.73	0.60	27	2.21	0.29	27	1.41	0.16	27	1.19	0.21

Study	Ho 1997
Design	RCT, parallel, single blind, 4 weeks, n 24, drop outs unclear.
Participants	USA, orthodontic patients, with fixed orthodontic appliances, 11 to 17 years (12M, 12F), GI > 2, no medical conditions.
Interventions	Sonicare Advance versus Oral-B P35, 2 minutes twice daily. Instructions. Timer supplied.
Outcome measures	Löe and Silness gingival index, Silness and Löe plaque index, bleeding on probing on 6 sites per bonded tooth at baseline and 4 weeks.
Notes	Manufacturer funded. No pre-examination instructions reported.

Results	Plaque Index						Gingival Index (L&S)					
	Baseline			Week 4			Baseline			Week 4		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Advance	12	2.65	0.38	12	1.15	0.17	12	2.00	0.00	12	1.42	0.27
Oral-B P35	12	2.58	0.33	12	2.33	0.44	12	2.02	0.07	12	1.96	0.14

Study	Yankell 1997
Design	RCT, parallel, single blind, 30 days, n 128 with 13 drop outs.
Participants	USA, adults, 18 to 50 years, > 18 teeth, no current orthodontic bands, no medical problems.
Interventions	Rowenta Plaque Dentacontrol Plus versus Sonicare Advance versus Braun Oral-B Ultra versus Oral-B P35, 2 min twice daily. Timer specified for powered.
Outcome measures	Turesky-modified Quigley and Hein plaque index, Eastman bleeding index and Löe and Silness (Lobene) gingival index on Ramfjord teeth at baseline, days 15 and 30. No soft tissue changes reported.
Notes	Participants asked to refrain from brushing 10 to 16 hours before evaluation.

Results

	Plaque Index						Gingival Index (L&S)					
	Baseline			Day 30			Baseline			Day 30		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Advance	31	2.69	0.46	31	2.720	0.44	31	2.280	0.22	31	2.130	0.20
Oral-B P35	28	2.56	0.51	28	2.660	0.44	28	2.300	0.35	28	2.140	0.32

Study	Nunn 2004
Design	RCT, parallel, single blind, 4 weeks, 200 subjects with 18 drop outs.
Participants	USA, adults, 18-68 years (71M, 111F), ≥ 20 teeth, plaque index ≥ 1.8, no medical problems affecting oral health, no severe gingivitis or periodontitis, no oral treatment needs.
Interventions	Sonicare Crest IntelliClean versus Oral-B 35 indicator manual. Detailed instructions, twice daily for 2 minutes. No other oral hygiene aids. Use of timer not stated.
Outcome measures	Pre-brush Turesky-modified Quigley & Hein plaque index at baseline and 4 weeks, safety, questionnaire.
Notes	Manufacturer funded. 14-20 hours of plaque accumulation. Crest liquid toothpaste for IntelliClean and Crest Cavity Gel for manual brush had same concentration of active ingredient sodium fluoride.

Results

	Plaque Index						Gingival Index
	Baseline			Week 4			
	n	Mean	SD	n	Mean	SD	n.a.
IntelliClean	93	2.44	0.42	93	2.22	0.60	
Oral-B Indicator 35	89	2.44	0.36	89	2.44	0.42	

Study	Cronin 2005
Design	RCT, parallel, 3 months, 109 subjects completed.
Participants	No data provided in abstract.
Interventions	Oral-B Sonic Complete versus manual, same toothpaste.
Outcome measures	Turesky-modified Quigley & Hein plaque index, Löe & Silness Gingival Index, safety.
Notes	Manufacturer funded. 12-18 hours of plaque accumulation. Information retrieved from IADR abstract and study summary leaflet from manufacturer (http://www.dentalcare.com/media/en-US/research_db/pdf/sonic/cronin_933.pdf).

Results

	Plaque Index						Gingival Index					
	Baseline			3 Months			Baseline			3 Months		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonic Complete	58	2.96	0.42	58	2.45	0.57	58	1.21	0.10	58	1.14	0.09
Manual (not specified)	51	2.92	0.46	51	2.65	0.46	51	1.20	0.09	51	1.16	0.10

Study	Chae 2007
Design	RCT, parallel, single blind, 12 weeks, 82 subjects completed.
Participants	South Korea, adults, 25-55 yrs, medically healthy, ≥ 20 teeth, PI ≥ 0.5, G I≥1, slight-moderate periodontitis (≥ 3 sites with 4-6 mm PPD, 1-4 mm AL, BOP)
Interventions	Sonicare Elite versus Butler #311, 2 minutes twice daily. Instructions. Use of timer not stated.
Outcome measures	Silness & Löe plaque index, Löe & Silness Gingival Index, probing pocket depth, bleeding on probing; whole mouth recording at baseline, 1,4,12 weeks.
Notes	Manufacturer funded. No pre-examination instructions reported. Information retrieved from IADR abstract and corresponding poster.

Results	Plaque Index						Gingival Index (L&S)					
	Baseline			Week 12			Baseline			Week 12		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Elite	52	1.38	0.33	52	0.64	0.37	52	1.33	0.29	52	0.65	0.40
Regular manual	30	1.45	0.31	30	1.12	0.37	30	1.45	0.28	30	1.14	0.40

Study	Holt 2007
Design	RCT, parallel, single blind, 4 weeks, 179 subjects with 4 drop outs.
Participants	UK, adults, 18-64 years (33M, 146F), non-smokers, ≥ 20 teeth, GI ≥ 2.0 at ≥ 20 sites, PI ≥ 0.8, no oral treatment needs, no severe gingivitis or periodontitis.
Interventions	Sonicare FlexCare versus Oral-B P40 manual. Twice daily for 2 minutes. Same toothpaste. No other oral hygiene aids. Detailed instructions. Compliance diary. Use of timer not stated.
Outcome measures	Silness & Löe plaque index, Löe & Silness Gingival Index, safety, compliance; measured at baseline, 2, 4 weeks.
Notes	Manufacturer funded. 3-6 hours of plaque accumulation. 4 week PI & GI (mean and SD) scores extracted from clinical study report.

Results	Plaque Index						Gingival Index					
	Baseline			Week 4			Baseline			Week 4		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare FlexCare	87	1.84	0.15	87	1.02	0.19	87	1.45	0.14	87	1.03	0.12
Oral-B P40	88	1.79	0.17	88	1.10	0.19	88	1.42	0.15	88	1.04	0.11

Study	Moritis 2008
Design	RCT, parallel, single blind, 4 weeks, 180 subjects with 12 drop outs.
Participants	UK, adults, 19-62 years (26M, 142F), non-smokers, ≥ 20 teeth, moderate gingival inflammation (GI ≥ 2.0 at ≥ 20 sites), PI≥0.8, no oral treatment needs, no severe gingivitis or periodontitis.
Interventions	Sonicare Elite versus Oral-B P40 manual. Twice daily for 2 minutes. Same toothpaste. No other oral hygiene aids. Detailed instructions. Compliance diary. Use of timer not stated.
Outcome measures	Silness & Löe plaque index, Löe & Silness Gingival Index, safety, compliance; measured at baseline, 2, 4 weeks.
Notes	Manufacturer funded. 3-6 hours of plaque accumulation. 4 week PI & GI (mean and SD) scores extracted from clinical study report.

Results	Plaque Index						Gingival Index					
	Baseline			Week 4			Baseline			Week 4		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Elite	81	1.55	0.26	81	0.68	0.18	81	1.38	0.17	81	0.81	0.14
Oral-B P40	87	1.48	0.25	87	0.79	0.18	87	1.36	0.17	87	0.90	0.14

Study	DeLaurenti 2008
Design	RCT, parallel, single blind, 4 weeks, 95 subjects (39M, 56F) with 3 drop-outs.
Participants	US orthodontic subjects; 12-42 yrs, routine MTB users; fixed braces on at least 10 teeth, each in the upper and lower arches; plaque index BBI > 2, full mouth GI < 2.5; no oral treatment needs.
Interventions	Sonicare FlexCare vs Oral-B P40 MTB (2 min, twice/day); instructions and supervised training for both treatments; Crest Cool Mint gel toothpaste; compliance diary.
Outcome measures	Modified Bonded Bracket Index (BBI); Turesky-modified Quigley and Hein plaque index on non-bracketed surfaces; full mouth Löe & Silness GI; safety; measured at baseline, 2, 4 weeks; 1 mild AE; safe to use.
Notes	Plaque scores for non-bracketed surfaces used for meta-analysis. Prophylaxis at baseline. 12-24 hrs plaque accumulation. Manufacturer funded.

Results	Plaque Index						Gingival Index					
	Baseline			Week 4			Baseline			Week 4		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare FlexCare	45	3.41	0.60	45	2.96	0.60	45	1.14	0.07	45	1.02	0.07
Oral-B P40	47	3.44	0.62	47	3.37	0.62	47	1.14	0.07	47	1.04	0.07

Study	DeLaurenti 2012
Design	RCT, parallel, single blind, 4 weeks, 144 subjects (51M, 93F) with 3 drop-outs
Participants	US; non-smoking, healthy subjects with mild to moderate gingivitis (GBI > 1 on 20 or more sites; PI > 1.8); 20+ natural teeth; 20-70 years; MTB users.
Interventions	Sonicare FlexCare+ with standard size DiamondClean brush head (2 min, twice/day) vs ADA-reference MTB (twice/day in habitual way); Crest Cool Mint Gel toothpaste; compliance diary provided.
Outcome measures	Turesky-modified Quigley and Hein plaque index (PI); modified gingival index (MGI); gingival bleeding index (GBI); measured at baseline, 2, 4 weeks; safe to use; no significant AE related to interventions.
Notes	Manufacturer funded. 3-6 hours of plaque accumulation prior to visits.

Results	Plaque Index						Gingival Index (MGI)					
	Baseline			Week 4			Baseline			Week 4		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Diamond Clean	70	2.77	0.40	70	1.81	0.58	70	2.08	0.40	70	1.55	0.47
ADA reference	72	2.85	0.38	71	2.60	0.41	72	2.14	0.39	71	1.74	0.48

Study	DeLaurenti 2013
Design	RCT, parallel, single blind, 4 weeks, 150 subjects (46M, 104F) with no drop-outs.
Participants	US, 18-64 yrs, routine MTB users, non-smoking, healthy subjects with mild to moderate gingivitis (GBI ≥ 1 on 20 or more sites; PI ≥ 1.8), 20+ natural teeth.
Interventions	Sonicare Platinum + InterCare compact brush head (2 min, twice/day) vs ADA reference MTB (subject's normal practice); Crest Cool Mint Gel toothpaste; compliance diary provided.
Outcome measures	Turesky-modified Quigley and Hein plaque index; modified gingival index (MGI); gingival bleeding index (GBI); measured at baseline, 2, 4 weeks; safety; no significant AEs; safe to use.
Notes	Manufacturer funded. 3-6 hours of plaque accumulation prior to visits.

Results	Plaque Index						Gingival Index (MGI)					
	Baseline			Week 4			Baseline			Week 4		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Platinum	75	2.75	0.35	75	2.01	0.46	75	2.06	0.46	75	1.36	0.45
ADA reference	75	2.81	0.35	75	2.83	0.29	75	2.10	0.43	75	1.98	0.44

Study	Swierkot 2013
Design	RCT, parallel trial, single blind, 12 months; 83 subjects (26M, 47F); 12 drop-outs.
Participants	Germany, 45-78 yrs, partially edentulous patients with at least one posterior implant, placed at least 12 months ago; current, regular MTB users. Systemically healthy, non-smoking; no generalized aggressive periodontitis or peri-implantitis or bone loss around natural teeth and implants >1mm in the year prior to the beginning of the study; no excessive calculus or tooth decay, oral dysfunctions, or contra-indicated medication.
Interventions	Sonicare FlexCare versus Oral-B P40 manual. MTB users instructed to use modified Bass technique, and Sonicare users according to DFU. All brushing for 2 minutes, twice daily. Colgate Total toothpaste.
Outcome measures	BOP, CAL, Löe & Silness Gingival Index, PPD, GR, Silness & Löe Plaque Index. Safe to use.
Notes	Mean number of implants per subject 4.3 (MTB group), 4.2 (Sonicare group). Data at 3 months extracted for short-term effects. Tooth scores used for overall analysis, implant scores used for implant-specific analysis. Manufacturer funded.

Results	Plaque Index						Gingival Index (L&S)					
	Baseline			3 Months			Baseline			3 Months		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare FlexCare	40	0.94	0.61	38	0.98	0.58	40	0.98	0.66	38	0.81	0.50
Oral-B P40	38	0.74	0.48	35	0.81	0.55	38	0.81	0.49	35	0.68	0.56

Study	Ward 2013
Design	RCT, parallel, single blind; 4 weeks; 148 subjects (47M, 101F); no drop-outs.
Participants	US, 18-65 yrs, routine MTB users; non-smoking, healthy subjects with mild to moderate gingivitis (GBI ≥ 1 on 20 or more sites; PI ≥ 1.8); 20+ natural teeth.
Interventions	Sonicare Platinum + InterCare standard brush head (2 min, twice/day) vs ADA reference MTB (subject's normal practice); Crest Cool Mint Gel toothpaste; compliance diary provided.
Outcome measures	Turesky-modified Quigley and Hein plaque index; modified gingival index; gingival bleeding index (GBI); measured at baseline, 2, 4 weeks; safety; no AEs reported; safe to use.
Notes	Manufacturer funded. 3-6 hours of plaque accumulation prior to visits.

Results	Plaque Index						Gingival Index (MGI)					
	Baseline			Week 4			Baseline			Week 4		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Platinum	74	2.80	0.36	74	1.95	0.51	74	2.00	0.35	74	1.29	0.50
ADA reference	74	2.82	0.40	74	2.82	0.37	74	2.09	0.42	74	2.00	0.47

Study	Zingler 2014
Design	RCT, four arm, parallel group, single blind, 12 weeks; 31-32 participants per group (55M, 63F) with 1-3 drop outs per group due to use of antibiotics or antibacterial rinses.
Participants	Germany; patients with fixed orthodontic appliances, 11-15 years. Healthy subjects with at least 10 fully erupted permanent teeth per arc, no recent use of antibiotic or antibacterial rinses, no carious lesions or early onset periodontitis.
Interventions	Four groups: 1) Sonicare FlexCare with ProResults brush head, 2) Manual (Elmex) + interdental brush (Curaprox), 3 + 4) Manual brush; groups 1-3 treated with a surface sealant prior to placement of ortho appliances. Instructed to brush twice daily with Elmex 1400ppm amine fluoride toothpaste. Stopwatch and diary to log brushing time.
Outcome measures	Plaque index bracket, Papillary bleeding index (PBI), Turesky-modification of Quigley and Hein plaque index (PI), modified approximal plaque index, DMFT/DMFS at baseline, 4, 8, 12 weeks.
Notes	Data for PI and PBI comparing groups 1 and 3 were extracted for further analysis. Reported medians and interquartile ranges were used to reconstruct approximate means and SDs since authors could not provide original data. Study did not receive external funding.

Results	Plaque Index						Gingival Index					
	Baseline			Week 12			Baseline			Week 12		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare FlexCare	28	1.20	1.17	28	1.01	0.69	28	0.62	0.53	28	0.72	0.32
Elmex	29	1.17	0.72	29	0.83	0.62	29	0.48	0.35	29	0.61	0.44

Study	Argosino 2015
Design	RCT, parallel, single blind; 4 weeks; 132 subjects (43M, 89F); 4 drop-outs.
Participants	US, 18-64 yrs, routine MTB users; non-smoking, healthy subjects with mild to moderate gingivitis (GBI ≥ 1 on 20 or more sites; PI ≥ 1.8); 20+ natural teeth.
Interventions	Sonicare 3-series with ProResults gum health brush head (2 min, twice/day) vs ADA reference MTB (habitual use, twice/day); Crest Cool Mint Gel toothpaste; compliance diary provided.
Outcome measures	Turesky-modified Quigley and Hein plaque index; modified gingival index; gingival bleeding index (GBI); measured at baseline, 2, 4 weeks; safe to use; no significant AE related to interventions.
Notes	Manufacturer funded. 3-6 hours of plaque accumulation prior to visits.

Results	Plaque Index						Gingival Index (MGI)					
	Baseline			Week 4			Baseline			Week 4		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare PS3	65	2.79	0.36	64	2.19	0.39	65	2.10	0.34	64	1.29	0.44
ADA reference	65	2.80	0.46	64	2.71	0.39	65	2.03	0.28	64	1.79	0.39

Study	Ward 2016
Design	RCT, parallel, single blind; 6 weeks; 154 subjects (43M, 111F); 11 drop-outs.
Participants	US, 19-64 yrs, routine MTB users; non-smoking, healthy subjects with mild to moderate gingivitis (GBI ≥ 1 on 20 or more sites; PI ≥ 1.8); 20+ natural teeth.
Interventions	Sonicare FlexCare Platinum with Adaptive Clean brush head (3 min Deep Clean Mode, twice/day) vs ADA reference MTB (habitual use); Crest Cool Mint Gel toothpaste; compliance diary provided.
Outcome measures	Turesky-modified Quigley and Hein plaque index; modified gingival index; gingival bleeding index (GBI); measured at baseline, 2, 6 weeks; safe to use; no significant AE related to interventions.
Notes	Manufacturer funded. 3-6 hours of plaque accumulation prior to visits.

Results	Plaque Index						Gingival Index (MGI)					
	Baseline			Week 6			Baseline			Week 6		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Platinum	75	2.84	0.48	72	1.52	0.76	75	2.16	0.40	72	1.18	0.49
ADA reference	73	2.90	0.53	71	2.94	0.62	73	2.27	0.45	71	2.27	0.48

Details of included studies with scores around implants, in chronological order

Study	Wolff 1998											
Design	RCT, parallel, single blind, 24 weeks, 31 subjects (16M, 15F), no drop-outs.											
Participants	US, 21-73 yrs, subjects with one or more restored dental implants, no antibiotic therapy or professional tooth cleaning in 3 months prior to trial. Systemically healthy, no contra-indicated medication, no dental treatment needs.											
Interventions	Oral hygiene instruction given (oral and written) on MTB (Crest Complete) or Sonicare Advance. Brush for 2 minutes, twice per day. MTB group was provided with timer. Oral hygiene instruction reinforced at each follow up visit (4, 8, 12 and 24 wks).											
Outcome measures	Silness and Löe plaque index, Löe and Silness gingival index, probing depth, bleeding index around implants. Questionnaire to assess compliance with and acceptance of assigned interventions.											
Notes	Prophy after baseline assessment and after 24 weeks assessment. Mean number of implants per subject 3.5 (MTB group), 2.8 (Sonicare group). Mean time since restoration of implant 2.5 yr (MTB), 0.5 yr (Sonicare). Mean time since original placement 3.51 yr (MTB), 1.16 yr (Sonicare). Data reported at 12 week visit extracted for analysis. Manufacturer funded.											
Results	Plaque Index						Gingival Index (L&S)					
	Baseline			Week 12			Baseline			Week 12		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare Advance	16	1.31	0.48	16	0.28	0.35	16	1.46	0.27	16	0.71	0.38
Crest Complete	15	1.27	0.47	15	0.53	0.44	15	1.58	0.42	15	0.93	0.41

Study	Swierkot 2013											
Design	RCT, parallel trial, single blind, 12 months; 83 subjects (26M, 47F); 12 drop-outs.											
Participants	Germany, 45-78 yrs, partially edentulous patients with at least one posterior implant, placed at least 12 months ago; current, regular MTB users. Systemically healthy, non-smoking; no generalized aggressive periodontitis or peri-implantitis or bone loss around natural teeth and implants >1mm in the year prior to the beginning of the study, no excessive calculus or tooth decay, oral dysfunctions, or contra-indicated medication.											
Interventions	Sonicare FlexCare versus Oral-B P40 manual. MTB users instructed to use modified Bass technique, and Sonicare users according to DFU. All brushing for 2 minutes, twice daily. Colgate Total toothpaste.											
Outcome measures	BOP, CAL, Löe & Silness Gingival Index, PPD, GR, Silness & Löe Plaque Index. Safe to use.											
Notes	Mean number of implants per subject 4.3 (MTB group), 4.2 (Sonicare group). Data at 3 months extracted for short-term effects. Tooth scores used for overall analysis, implant scores used for implant-specific analysis. "Supported by a grant from Philips healthcare systems"											
Results	Plaque Index						Gingival Index (L&S)					
	Baseline			3 Months			Baseline			3 Months		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Sonicare FlexCare	42	0.86	0.73	40	0.87	0.73	42	0.91	0.68	40	0.84	0.60
Oral-B P40	41	0.56	0.52	38	0.74	0.61	41	0.85	0.83	38	0.83	0.70

Study	Lee 2015											
Design	RCT, parallel, single blind, 2 months, 40 subjects (23M, 17F); 0 drop outs.											
Participants	South Korea, 27-75 yrs, systemically healthy patients with at least one implant restoration, installed at least 3 months previously; presence of peri-implant mucositis; no recent antibiotic use or contra-indicated medication, no dental treatment needs.											
Interventions	Brushing three times per day for two minutes using Bass technique with MTB (Butler GUM 311) or manufacturer's instructions for Sonicare DiamondClean. Subjects recorded brushing duration and frequency.											
Outcome measures	Modified plaque index (mPI), modified sulcus bleeding index (mSBI) for implant sites at 0, 1 and 2 months. Safe to use. Both groups compliant in reported brushing behaviors.											
Notes	Mean number of implants per subject 1.7 (MTB group), 1.5 (Sonicare group). Mean time since restoration of implant 5.6 yr (MTB), 4.2 yr (Sonicare). Mean time since original placement 6.4 yr (MTB), 6.2 yr (Sonicare). Data for mSBI provided by authors upon request; mPI data extracted from paper. Supported by a grant from Philips.											
Results	Plaque Index						Gingival Index					
	Baseline			2 Months			Baseline			2 Months		
	n	Mean	SD	n	Mean	SD	n	Mean	SD		Mean	SD
Sonicare Diamond Clean	20	1.70	0.65	20	0.43	0.68	20	1.40	0.68	20	0.47	0.63
Butler GUM 311	20	1.85	0.62	20	1.09	0.95	20	1.46	0.67	20	0.88	0.65

Annex 2
Statistical Approach Comparing Sonic vs. Rotating-Oscillating Toothbrushes

Method:

Since we followed the Cochrane approach, their reported comparison of rotating-oscillating with manual toothbrushes may be used to compare our results with. Assuming the manual toothbrush groups in both meta-analyses are comparable in interpretation (because in both cases a variety of manual toothbrushes was used), we can use the reported data to also give an estimate of the difference between sonic and rotating-oscillating toothbrushes. For this, we regard the SMD as the difference in means (SM) of some standardized quantity measured for each group separately (sonic (S), rotating-oscillating (R), manual (M)). Then the difference in SMDs of the two analyses is a measure for the difference between sonic and rotating-oscillating toothbrushes: . The meta-analysis provides standard errors of and , so that the standard error of their difference is obtained by . The is obtained directly from the meta-analysis; it is directly related to the confidence interval of SMD by . Using the same formula we calculate the confidence interval for . A test for difference between sonic and rotating-oscillating toothbrushes is then obtained by a Z-test using the estimate and standard error.

Results:

	R vs *M*		*S* vs *M*		*S* vs *R*				
Outcome	SMD	SE	SMD	SE	SMD	SE	Z	p-value	95% CI
Plaque	-0.53	0.11	-0.89	0.20	-0.37	0.22	-1.64	0.10	[-0.80. 0.07]
Gingivitis	-0.49	0.12	-0.67	0.18	-0.17	0.21	-0.82	0.41	[-0.59, 0.24]

Conclusion:

Thus, results for plaque removal were suggestive of a favorable effect for sonic over rotating-oscillating toothbrushes with [95%CI] = -0.37 [-0.80, 0.07] (p = 0.10), whereas gingivitis reduction was comparable with = -0.17 [-0.59, 0.24] (p = 0.41).

A Comparison of the Effect of Two Power Toothbrushes on the Gingival Health and Plaque Status of Subjects with Moderate Gingivitis

Michelle Starke, PhD Marcia Delaurenti, RDH, MS Marilyn Ward, DDS Sonia Souza, PhD

Philips Healthcare
Bothell, WA, USA

Kimberly R. Milleman, RDH, BSEd, MS Jeffery L. Milleman, DDS, MPA

Salus Research
Ft. Wayne, IN, USA

Abstract

- **Objective:** To compare the effect of the Philips Sonicare DiamondClean plus Premium plaque control brush head with the Oral-B 7000 plus CrossAction brush head on gingivitis and supragingival plaque reduction following a 42-day period of home use.
- **Methods:** This was a randomized, parallel, examiner-blind, prospective clinical trial conducted on generally healthy subjects. Eligible subjects met the following eligibility criteria: age 18–65, non-smoker, routine manual toothbrush user, ≥ 50 sites of gingival bleeding per the Gingival Bleeding Index (GBI), and ≥ 1.8 plaque score per the Modified Plaque Index (MPI), assessed three to six hours following the last oral hygiene procedure. Eligible subjects were enrolled in the study and randomly assigned to use either a Philips Sonicare DiamondClean with Premium plaque control brush head power toothbrush (SPC) or an Oral-B® 7000 with CrossAction™ brush head power toothbrush (OCA), for twice daily home use over a period of 42 days. All subjects were dispensed a standard fluoride-containing dentifrice and both toothbrushes were to be used in their respective Deep Clean modes. Safety and efficacy evaluations were performed at 14 and 42 days following Baseline.
- **Results:** Two-hundred eighty-four subjects completed this trial (142 subjects per treatment group). Least squares mean (95% CI) estimates for reduction and percent reduction of gingivitis per Modified Gingival Index (MGI) following 42 days of product use for the SPC group were 1.17 (1.10, 1.24) and 45.68% (42.95%, 48.40%); for the OCA group they were 0.69 (0.62, 0.76) and 26.83% (24.10%, 29.56%). The mean difference (95% CI) between the two treatment groups was 0.48 (0.38, 0.58) and 18.85% (14.99%, 22.70%) for reduction and percent reduction, respectively. The lower limit of the 95% CI for the difference in Overall score between the two treatment groups was greater than the pre-defined non-inferiority margin (*i.e.*, -0.10 or -5%); therefore SPC was declared non-inferior to OCA. In addition, since the 95% CI for the difference did not include zero, SPC was declared superior to OCA in the reduction of gingivitis per MGI at Day 42 (p-value < 0.0001). Similarly, for MGI at Day 14 and for GBI and MPI at Day 14 and Day 42, significantly larger reductions were observed for SPC compared to OCA (p-value < 0.0001).
- **Conclusions:** Philips Sonicare DiamondClean with Premium plaque control brush head (SPC) was statistically superior to the Oral-B 7000 with CrossAction brush head (OCA) in reducing gingival inflammation, gingival bleeding, and supragingival plaque following 14 and 42 days of home use. Both products were safe for use.

(J Clin Dent 2017;28(Spec Iss A):A29–35)

Introduction

The progression from periodontal health to disease is influenced by multiple factors.[1] One of the key factors driving and defining periodontal status is the accumulation of plaque on tooth surfaces.[2] Dental plaque is comprised of a community of microbes and their associated byproducts assembled in a biofilm matrix.[3] Biofilms have an evolutionary history documented in the fossil record, and exist in an array of environments and under highly varied conditions.[4] The character and constituents of oral biofilms can have an effect on the expression of adjacent host tissues as healthy and thriving, as irritated and inflamed, or as tissue compromised by disease.[5-7]

As these oral microbial communities are dynamic, daily mechanical removal is necessary to limit the amount of accumulated plaque. A simple consequence of mechanical removal affects the character of oral biofilms.[8] Together, reducing the burden of plaque regrowth with its resultant impact on the species and byproducts within the biofilm, help to preserve and sustain periodontal health.[9]

While manual toothbrushes are certainly effective tools for mechanically sweeping away plaque, there continues to be a growing body of evidence that demonstrates the oral health benefits borne out of innovations in the power toothbrush category.[10] Power toothbrush technology, in general, grew from the observation that manual devices are fundamentally limited by the dexterity, compliance, and engagement of the user. While patients may habitually brush their teeth twice a day as counselled by the dental professional, they may not brush for a sufficient length of time or with adequate precision to have the intended effect of comprehensive plaque removal on all tooth sites. As a result, sites that harbor plaque over long periods can become problem sites,[11] putting the associated periodontium and tooth structures at risk for disease.

Powered toothbrushes aid the user in improving on the efficacy of mechanical cleaning by incorporating a number of features. These include timing prompts, powerful motors to drive brush

head motion, and brush head designs that target specific problems based on a patient's needs. The Philips Sonicare (Philips Oral Healthcare, Bothell, WA, USA) and Oral-B® (Procter & Gamble, Cincinnati, OH, USA) platforms of powered toothbrushes include these features and have been clinically demonstrated to be both safe and effective.[12-16] These products differ, however, in the mechanical action that drives brush head motion. While the Sonicare platform drives high-frequency, high-amplitude brush head motion, the Oral-B platform is characterized by an oscillating, rotating, and pulsating movement.

The current clinical trial was conducted to compare two marketed power toothbrushes, the Philips Sonicare DiamondClean power toothbrush with Premium plaque control* brush head and the Oral-B® 7000 with CrossAction™ brush head and SmartGuide accessory. The clinical endpoints measured included a comparison of the effects of 42 days of product use on plaque, gingival inflammation, and gingival bleeding. (*Note: brush head was previously named AdaptiveClean, renamed to Premium plaque defense in certain countries.)

Materials and Methods

Study Design and Objectives

This was a prospective, randomized, single-center, parallel study designed to compare the efficacy and safety of two power toothbrushes; the Philips Sonicare DiamondClean with Premium plaque control brush head (SPC), and the Oral-B 7000 with CrossAction brush head and SmartGuide accessory (OCA). Efficacy and safety were assessed following 14 and 42 days of home use of the study products. Figure 1 depicts the procedures and visit timeline of the study.

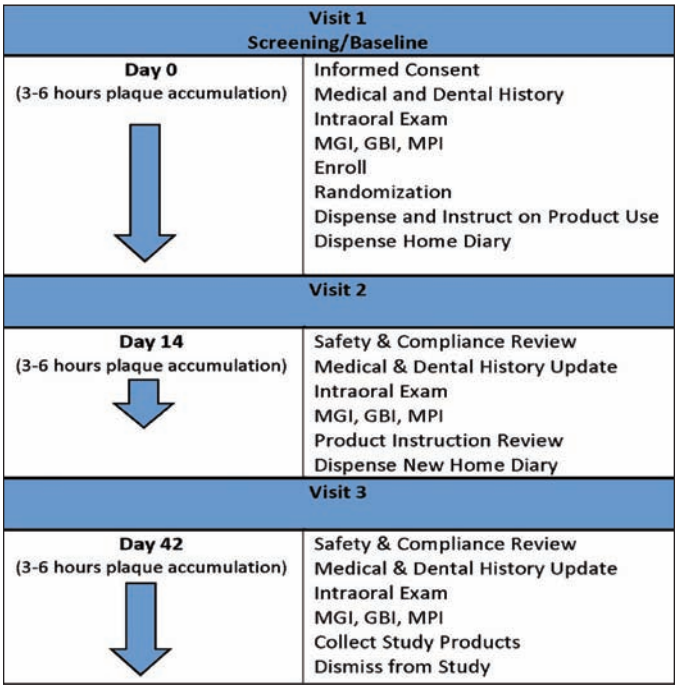

Figure 1. *Study visits and procedures.*

The primary objective of the study was to compare the reduction in gingivitis, per the Modified Gingival Index[17] (MGI), following 42 days of home use. Secondary objectives included the following comparisons between products: reduction in MGI following 14 days of use; reduction in surface plaque following 14 and 42 days of product use; reduction in gingival bleeding following 14 and 42 days of product use; and safety of the study regimens. Additionally, the proportion of subjects with improvement in these endpoints were compared at each evaluation.

Subjects

This study was reviewed and approved by the Chesapeake Investigational Review Board (Pro00018071). Eligible subjects were generally healthy manual toothbrush users who were 18–65 years of age, non-smokers, able to provide Informed Consent, and follow the study procedures. The study population included subjects exhibiting moderate gingivitis, with ≥ 50 sites of bleeding per the Gingival Bleeding Index (GBI)[18] and a plaque score of ≥ 1.8 per the Lobene and Soparker Modified Plaque Index (MPI)[19,20] assessed at three to six hours following the last oral hygiene procedure. Subjects with rampant decay, significant gingival recession, evidence of periodontitis, or heavy deposits of calculus were not included in the study panel.

In the event that a subject required dental or medical care in a context that could affect a safety or efficacy endpoint of the study, or which put the subject at greater risk, the participant was removed from the study at the discretion of the study investigator.

Efficacy and Safety Measurements

Efficacy was evaluated by examiners trained in the visual assessment of plaque and gingivitis per published visual clinical metrics. In this study, the following measurement methods were utilized: Lobene and Soparker Modified Plaque Index (MPI); the Modified Gingival Index (MGI); and the Gingival Bleeding Index (GBI). Table I provides the scale and score descriptors per Index. To minimize bias, the study examiners who performed the efficacy evaluations were blinded to the treatment assignment of each subject.

Safety was assessed by oral tissue exam at each clinic visit, and by subject report per home diary record.

Randomization and Treatment Groups

Following Informed Consent and assessment of eligibility, enrolled subjects were randomized. Subjects received either a Sonicare DiamondClean with Premium plaque control brush head (SPC) power toothbrush or an Oral-B 7000 with CrossAction brush head power toothbrush including the SmartGuide accessory (OCA). Randomization was balanced for gender such that approximately equal numbers of males and females were represented in each treatment group. All subjects were dispensed a standard fluoride-containing dentifrice and were instructed to utilize the assigned product according to the manufacturer's Deep Clean mode instructions. The intercurrent use of any other oral hygiene device or medicament was prohibited during the study period.

Upon completion of all procedures at the Day 42 visit, subjects returned the assigned test products and were dismissed from the study.

Data Capture

Study data were captured on a web-based data system with programmed logic and edit-checks. To appropriately maintain the integrity of the data, access to the system was limited by log-in credentials that matched the study role of the user. Study data were monitored to ensure accuracy of recording and reporting.

Statistical Methods

Sample Size Determination. The study was designed to test the

Table I
Scoring Methodology for Efficacy Metrics; Plaque, Gingival Inflammation, and Gingival Bleeding

Lobene and Soparker Modified Plaque Index, 6 sites per tooth, excluding 3rd molars					
0	1	2	3	4	5
No plaque	Separate flecks of plaque at the gingival margin	A thin continuous band of plaque (up to 1mm) at the cervical margin of the tooth	A band of plaque wider than 1 mm but covering less than 1/3 of the crown of the tooth	Plaque covering at least 1/3 but less than 2/3 of the crown of the tooth	Plaque covering 2/3 or more of the tooth
Modified Gingival Index, 6 sites per tooth, excluding 3rd molars					
0	1	2	3	4	N/A
Absence of inflammation	Mild inflammation, slight change in color, little change in texture of any portion of but not the entire margin or papillary gingival unit	Mild inflammation but involving the entire margin or papillary unit	Moderate inflammation; glazing, redness, edema and/or hypertrophy of margin or papillary unit	Severe inflammation; marked redness, edema and/or hypertrophy or marginal or papillary gingival unit, spontaneous bleeding, congestion or ulceration	
Gingival Bleeding Index, 6 sites per tooth, excluding 3rd molars					
0	1	2	3	N/A	N/A
No bleeding	Bleeding on gently probing	Bleeding appears immediately upon gently probing	Spontaneous bleeding which is present prior to probing		

hypothesis that gingivitis reduction and plaque removal for the DiamondClean power toothbrush with Premium plaque control brush head was non-inferior to that obtained when brushing with Oral-B 7000 power toothbrush with CrossAction brush head. Based on prior studies in which a Sonicare power toothbrush was compared to the standard of care manual tooth brushing, we assumed that a minimum clinically significant difference in plaque and gingivitis reduction by a margin of -0.20 or 10% was sufficient to differentiate the products. For this study, if the difference between the two power toothbrushes was less than 0.10 and 5% (*i.e.*, 50% of the difference between the power toothbrush and MTB), for reduction and percent reduction, respectively, the two power toothbrushes were to be assumed of similar efficacy (*i.e.*, non-inferior).

In order to establish the non-inferiority for the primary efficacy variable with a one-sided type I error of 2.5% with 80% power, approximately 290 subjects were required to be evaluated (145 subjects per treatment group). This calculation was based on a non-inferiority margin of 5% (percent reduction in Overall MGI) and 0.10 (in Overall MGI reduction) and assumed a true mean difference of zero between the OCA and SPC, with a common standard deviation (SD) of 15% (MGI percent reduction) and 0.30 (in Overall MGI reduction).

To account for an attrition rate of about 10%, approximately 324 (*i.e.*, 162 subjects per group) were to be randomized with a target to complete 290 evaluable subjects (145 subjects per group).

General Considerations

The primary efficacy analysis was performed including all randomized subjects with Baseline and Day 42 gingivitis evaluations (modified intent to treat, mITT). Subjects were analyzed according to the randomized treatment assignment. The analysis of safety included all randomized subjects.

Continuous variables were summarized using the number of non-missing observations, mean, standard deviation (SD), 95% confidence interval (CI) of the mean, median, minimum, and maximum; categorical variables were summarized using the frequency count and the percentage of subjects in each category. All analyses were conducted using SAS® software.

Demographics and Baseline Characteristics

Standard subject demographics (*e.g.*, age, gender) were summarized for all mITT subjects by treatment group and Overall. For continuous subject characteristics, means were compared between groups using one way analysis of variance (ANOVA). The incidence of the categorical variables were compared using the Chi-square test or Fisher's exact test as appropriate.

Efficacy Endpoints

The efficacy indices, MGI, GBI, and MPI, at each tooth site, were scored using the scoring methodology described in Table I. A standardized data collection form was used to capture these data at each study visit. For each index, three summary scores were used as efficacy endpoints. These included: the Overall score, calculated as the sum of scores at all evaluable sites divided by the number of evaluable sites; reduction from Baseline, calculated as the Baseline score minus the post-baseline score; and percent reduction from Baseline, calculated as the reduction in score divided by the Baseline score times 100.

All three summary scores were considered as continuous variables and summarized for the whole mouth (Overall) and by region of the mouth (*i.e.*, anterior, posterior, interproximal, and posterior interproximal). Analyses were performed separately for each summary score and for each region. For brevity, sub-region analysis is not reported here.

Primary Efficacy Analysis

The primary efficacy measure for this study was the reduction in gingivitis score from Baseline to Visit 3 (Day 42). The efficacy analysis was performed on the mITT population, which included all randomized subjects with an MGI score at Baseline and Day 42. Comparison between the two treatment groups for reduction and percent reduction from Baseline was performed using a linear model with the Baseline score as a covariate. The following hypothesis was evaluated:

$$H_o: \mu_{Sonicare} - \mu_{Oral\text{-}B} \leq -\Delta$$
$$H_a: \mu_{Sonicare} - \mu_{Oral\text{-}B} > -\Delta$$

where $-\Delta$ is the non-inferiority margin of -5% (percent reduction in Overall MGI) and -0.10 (Overall MGI reduction) and μ is the mean

MGI reduction or percent reduction. The non-inferiority approach is a well-documented statistical methodology used in clinical trials, including for use in US FDA investigational drug, new drug, and biologics licensing applications.[21,22]

Least squares mean (LSM), standard error (SE) of the mean, and two-sided 95% confidence intervals (CI) were presented by treatment group. A two-sided 95% CI for the mean difference between the two treatment groups was constructed. If the lower limit 95% CI for the difference between the two treatment groups was found to be greater than the pre-defined non-inferiority margin of -5% or -0.10, the SPC was to be declared non-inferior to OCA. Also, if the lower limit of the 95% CI for the treatment difference between the two toothbrushes was greater than zero, the SPC was to be declared superior to the OCA.

Secondary Efficacy Analysis

Secondary efficacy variables were: reduction of gingivitis following 14 days of home use; reduction in plaque score and gingival bleeding; the percent of bleeding sites and the number of bleeding sites post 14 and 42 days of home use; the proportion of subjects with improved gingivitis; reduced gingival bleeding; and plaque removal post 14 and 42 days of home use. Analyses evaluating the reduction of gingivitis, plaque, and gingival bleeding were performed for each time point (*i.e.*, post 14 and 42 days of use) using a similar method as described above for the primary endpoint.

In order to assess the proportion of subjects with improved gum health per MGI, subjects were defined as having improved gingival health at Days 14 and 42 if their percent reduction in MGI was greater than or equal to 20%. The proportion and 95% CI of subjects with improved gingival health were presented. A similar analysis, using the same 20% cut-off value, was performed for reduced gingival bleeding (per GBI) and reduced plaque (per MPI).

Results

Demographics

Three-hundred and twelve subjects provided Informed Consent and were screened for this study. Of these, 304 were enrolled and randomized, and 284 subjects completed the study (142 subjects per treatment group). Twenty subjects did not complete the study (eight subjects withdrew, 12 were lost to follow-up) and were thus not included in the efficacy analysis. Table II provides a summary of demographic information of randomized subjects who were included in the mITT population. The mean (SD) age of mITT subjects was 38.6 (12.0) years, with 213 female (75.0%), and 71 (25.0%) male participants. There were no significant differences in the age and gender distribution among the two treatment groups.

Table II

Demographic Characteristics, Modified Intent to Treat Subjects

Parameter	Category	Treatment: Sonicare + Premium Plaque Control	Treatment: Oral B 7000 + CrossAction	Total	p-value
Age (yrs.)	No. Subjects	142	142	284	0.5957
	Mean(SD)	38.2 (12.4)	39.0 (11.7)	38.6 (12.0)	
	95% CI	(36.2, 40.3)	(37.1, 40.9)	(37.2, 40.0)	
	Median	38	38	38	
	Min, Max	(18, 65)	(18, 64)	(18, 65)	
Gender	Female	106 (74.6%)	107 (75.4%)	213 (75.0%)	0.8910
	Male	36 (25.4%)	35 (24.6%)	71 (25.0%)	

Primary Efficacy Results

Modified Gingival Index. The distribution of the Overall MGI mean score by treatment group is presented in Figure 2 as a boxplot, which depicts the following: the upper whisker indicates the maximum observed value; the upper boundary of the box marks the 75th percentile of observed values; the line intersecting the box indicates the median; the circle within the box indicates the mean; the lower boundary of the box marks the 25th percentile of observed values; and the lower whisker denotes the minimum observed value. Both treatment groups had a similar distribution at Baseline (*i.e.*, mean Overall MGI score of 2.6). Also, the median at Baseline was 2.64 for SPC and 2.68 for OCA, indicating that the data were normally distributed.

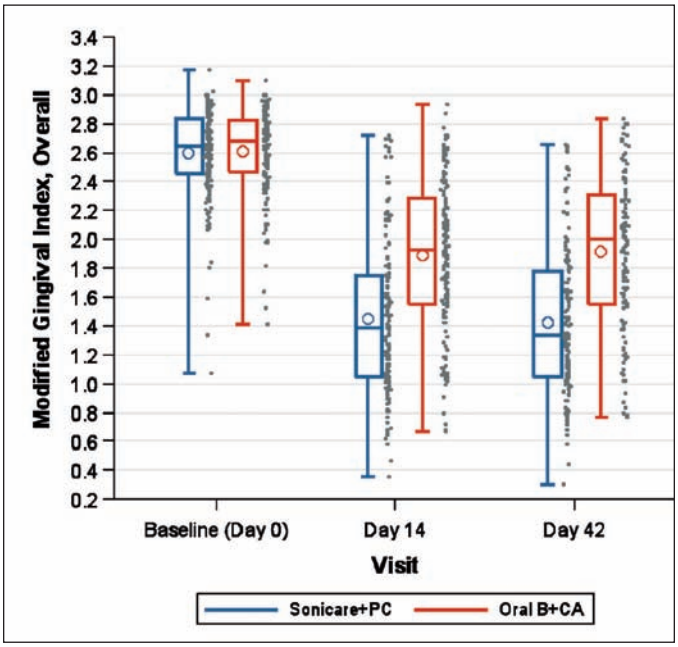

Figure 2. *Boxplot of Modified Gingival Index, overall, by treatment group at Baseline, Day 14, Day 42. Note: Each dot represents a single observation.*

The MGI outcomes at Baseline, Day 14, and Day 42, including reduction and percent reduction from Baseline, as well as the analysis presenting the percentage of subjects with ≥ 20% reduction in MGI, by treatment group, are presented in Table III.

For the primary efficacy endpoint (MGI at Day 42), the Overall LSM reduction and percent reduction (95% CI) was 1.17 (1.10, 1.24) and 45.68% (42.95%, 48.40%), respectively for SPC, and 0.69 (0.62, 0.76) and 26.83% (24.10%, 29.56%), respectively for OCA.

At Day 14, the Overall LSM reduction and percent reduction (95% CI) was 1.14 (1.07, 1.22) and 44.73% (42.00%, 47.45%), respectively for SPC, and 0.72 (0.65, 0.79) and 27.92% (25.20%, 30.64%), respectively for OCA.

For Day 42, the LSM for the difference in Overall MGI score between the two treatment groups was 0.48 (0.38, 0.58) and 18.85% (14.99%, 22.70%), for reduction and percent reduction, respectively. Similarly, for Day 14, the LSM for the difference in Overall MGI score between the two treatment groups was 0.42 (0.32, 0.53) and 16.81% (12.95%, 20.66%), for reduction and percent reduction, respectively. For both time points, the lower limit of the 95% CI for the difference was greater than the pre-defined non-inferiority margin (*i.e.*, -0.10 or -5%), therefore SPC was declared non-inferior to the OCA. In addition, since the 95% CI for the difference does not include zero,

SPC was declared superior to OCA in reduction of gingivitis (p-value < 0.0001, for both time points).

For the proportion analysis, at Day 14, the proportion of subjects with gingival health that improved by a margin of 20% (95% CI) or more was 88.7% (82.3%, 93.4%) for SPC and 59.9% (51.3%, 68.0%) for OCA. At Day 42, these outcomes were 92.3% (86.6%, 96.1%) for SPC and 64.1% (55.6%, 72.0%) for OCA.

Table III
Modified Gingival Index, Reduction, Percent Reduction and Proportion Analysis, Overall, at Baseline, Day 14, Day 42

Variable	Statistic	Treatment: Sonicare + Premium Plaque Control	Treatment: Oral B + CrossAction	Difference	p-value
Baseline (Day 0)	No Subjects	142	142		
	LS Mean (SE)	2.60 (0.03)	2.61 (0.03)	-0.01 (0.04)	0.7174
	95% CI	(2.55, 2.65)	(2.56, 2.66)	(-0.09, 0.06)	
Day 14	LS Mean (SE)	1.46 (0.04)	1.89 (0.04)	-0.42 (0.05)	<.0001
	95% CI	(1.39, 1.53)	(1.81, 1.96)	(-0.53, -0.32)	
Reduction from Baseline	LS Mean (SE)	1.14 (0.04)	0.72 (0.04)	0.42 (0.05)	<.0001
	95% CI	(1.07, 1.22)	(0.65, 0.79)	(0.32, 0.53)	
Percent Reduction from Baseline	LS Mean (SE)	44.73(1.38)	27.92(1.38)	16.81(1.96)	<.0001
	95% CI	(42.00, 47.45)	(25.20, 30.64)	(12.95, 20.66)	
MGI PRFB[a] >=20%	n(Prop)	126 (88.7%)	85 (59.9%)		
	95% CI	(82.3%, 93.4%)	(51.3%, 68.0%)		
Day 42	LS Mean (SE)	1.43 (0.04)	1.91 (0.04)	-0.48 (0.05)	<.0001
	95% CI	(1.36, 1.50)	(1.84, 1.98)	(-0.58, -0.38)	
Reduction from Baseline	LS Mean (SE)	1.17 (0.04)	0.69 (0.04)	0.48 (0.05)	<.0001
	95% CI	(1.10, 1.24)	(0.62, 0.76)	(0.38, 0.58)	
Percent Reduction from Baseline	LS Mean (SE)	45.68(1.39)	26.83(1.39)	18.85 (1.96)	<.0001
	95% CI	(42.95, 48.40)	(24.10, 29.56)	(14.99, 22.70)	
MGI PRFB[a]>=20%	n(Prop)	131 (92.3%)	91 (64.1%)		
	95% CI	(86.6%, 96.1%)	(55.6%, 72.0%)		

[a] PRFB = Percent Reduction from Baseline

Secondary Efficacy Results

Gingival Bleeding Index. The distribution of Overall GBI mean score by treatment group is presented in Figure 3. Both treatment groups had a similar distribution at Baseline (*i.e.*, mean Overall GBI score of 0.53 and 0.54 for SPC and OCA, respectively). Also, the median at Baseline was 0.48 for SPC and 0.49 for OCA, indicating that the data may have a minor deviation from normality.

The GBI outcomes at Baseline, Day 14, and Day 42, including reduction and percent reduction from Baseline, as well as the analysis presenting the percentage of subjects with ≥ 20% reduction in GBI by treatment group, are presented in Table IV.

At Day 14, the LSM for reduction and percent reduction in Overall GBI (95% CI) was 0.36 (0.34, 0.38) and 66.75% (62.78%, 70.72%), respectively for SPC and 0.26 (0.24, 0.28) and 49.38% (45.40%, 53.35%), respectively for OCA.

At Day 42, the LSM for reduction and percent reduction in GBI (95% CI) was 0.40 (0.39, 0.42) and 75.81% (72.78%, 78.84%), respectively for SPC and 0.31 (0.30, 0.33) and 58.76% (55.73%, 61.79%), respectively for OCA.

At both time points (Day 14 and Day 42), SPC was declared superior to OCA in reducing gingival bleeding, with p-values of < 0.0001 for both reduction and percent reduction in GBI.

Also, at Day 14, the proportion of subjects with gingival bleeding that improved by a margin of 20% (95% CI) or more was 95.8% (91.0%, 98.4%) for SPC and 89.4% (83.2%, 94.0%) for OCA. At Day 42, these outcomes were 100% (97.4%, 100%) for SPC and 95.1% (90.1%, 98.0%) for OCA.

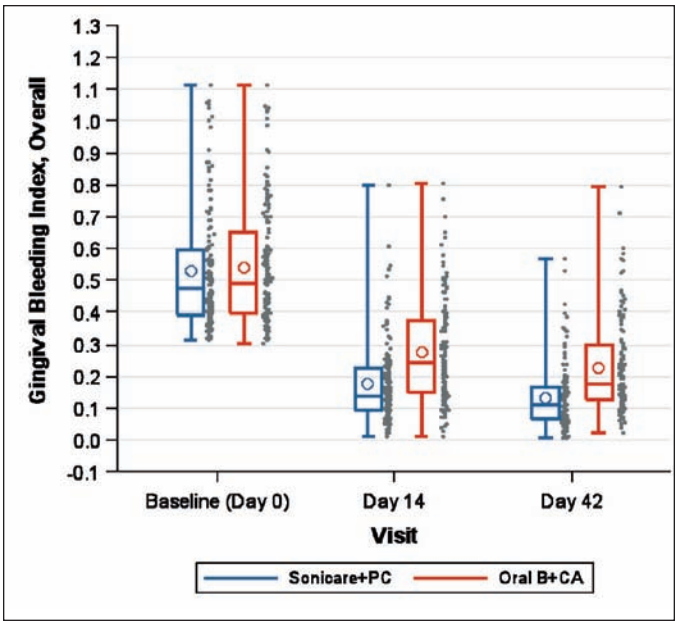

Figure 3. *Boxplot of Gingival Bleeding Index, overall, by treatment group at Baseline, Day 14, Day 42. Note: Each dot represents a single observation.*

Table IV
Gingival Bleeding Index, Reduction, Percent Reduction and Proportion Analysis, Overall, at Baseline, Day 14, Day 42

Variable	Statistic	Treatment: Sonicare + Premium Plaque Control	Treatment: Oral B + CrossAction	Difference	p-value
Baseline (Day 0)	No Subjects	142	142		
	LS Mean (SE)	0.53 (0.02)	0.54 (0.02)	-0.01 (0.02)	0.5986
	95% CI	(0.50, 0.56)	(0.51, 0.57)	(-0.06, 0.03)	
Day 14	LS Mean (SE)	0.18 (0.01)	0.27 (0.01)	-0.10 (0.01)	<.0001
	95% CI	(0.16, 0.20)	(0.25, 0.29)	(-0.13, -0.07)	
Reduction from Baseline	LS Mean (SE)	0.36 (0.01)	0.26 (0.01)	0.10 (0.01)	<.0001
	95% CI	(0.34, 0.38)	(0.24, 0.28)	(0.07, 0.13)	
Percent Reduction from Baseline	LS Mean (SE)	66.75 (2.02)	49.38 (2.02)	17.37 (2.85)	<.0001
	95% CI	(62.78, 70.72)	(45.40, 53.35)	(11.75, 22.99)	
GBI PRFB[a] >=20%	n(Prop)	136 (95.8%)	127 (89.4%)		
	95% CI	(91%, 98.4%)	(83.2%, 94.0%)		
Day 42	LS Mean (SE)	0.13 (0.01)	0.22 (0.01)	-0.09 (0.01)	<.0001
	95% CI	(0.12, 0.15)	(0.21, 0.24)	(-0.11, -0.07)	
Reduction from Baseline	LS Mean (SE)	0.40 (0.01)	0.31 (0.01)	0.09 (0.01)	<.0001
	95% CI	(0.39, 0.42)	(0.30, 0.33)	(0.07, 0.11)	
Percent Reduction from Baseline	LS Mean (SE)	75.81 (1.54)	58.76 (1.54)	17.05 (2.18)	<.0001
	95% CI	(72.78, 78.84)	(55.73, 61.79)	(12.76, 21.34)	
GBI PRFB[a]>=20%	n(Prop)	142 (100%)	135 (95.1%)		
	95% CI	(97.4%, 100%)	(90.1%, 98.0%)		

[a] PRFB = Percent Reduction from Baseline

Modified Plaque Index. The distribution of Overall MPI mean score by treatment group is presented in Figure 4. Both treatment groups had a similar distribution at Baseline (*i.e.*, mean Overall MPI score of 2.9). Also, the median at Baseline was 2.87 for SPC and 2.93 for OCA, indicating that the data were normally distributed.

The MPI outcomes at Baseline, Day 14, and Day 42, including reduction and percent reduction from Baseline, as well as the analysis

presenting the percentage of subjects with ≥ 20% reduction in MPI by treatment group, are presented in Table V.

At Day 14, the LSM for reduction and percent reduction in Overall MPI score (95% CI) was 1.13 (1.05, 1.20) and 38.68% (36.19%, 41.16%), respectively for SPC and 0.54 (0.47, 0.61) and 18.28% (15.79%, 20.77%), respectively for OCA.

At Day 42, the LSM for reduction and percent reduction in Overall MPI (95% CI) was 1.11 (1.03, 1.18) and 37.58% (35.10%, 40.05%), respectively for SPC and 0.60 (0.53, 0.67) and 20.70% (18.22%, 23.17%), respectively for OCA.

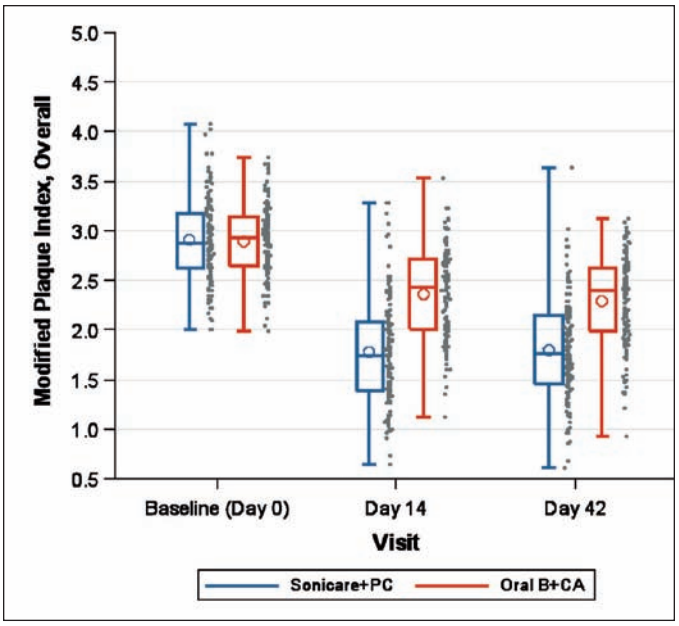

Figure 4. *Boxplot of Modified Plaque Index, Overall, by Treatment Group at Baseline, Day 14, Day 42. Note: Each dot represents a single observation.*

Table V
Modified Plaque Index, Percent Reduction and Proportion Analysis, Overall, at Baseline, Day 14, Day 42

Variable	Statistic	Treatment: Sonicare + Premium Plaque Control	Treatment: Oral B + CrossAction	Difference	p-value
Baseline (Day 0)	No Subjects	142	142		
	LS Mean (SE)	2.90 (0.03)	2.90 (0.03)	0.00 (0.05)	0.9777
	95% CI	(2.84, 2.97)	(2.84, 2.97)	(-0.09, 0.09)	
Day 14	LS Mean (SE)	1.78 (0.04)	2.36 (0.04)	-0.59 (0.05)	<.0001
	95% CI	(1.70, 1.85)	(2.29, 2.44)	(-0.69, -0.49)	
Reduction from Baseline	LS Mean (SE)	1.13 (0.04)	0.54 (0.04)	0.59 (0.05)	<.0001
	95% CI	(1.05, 1.20)	(0.47, 0.61)	(0.49, 0.69)	
Percent Reduction from Baseline	LS Mean (SE)	38.68 (1.26)	18.28 (1.26)	20.40 (1.79)	<.0001
	95% CI	(36.19, 41.16)	(15.79, 20.77)	(16.88, 23.91)	
MPI PRFB[a]>=20%	n(Prop)	124 (87.3%)	59 (41.5%)		
	95% CI	(80.7%, 92.3%)	(33.3%, 50.1%)		
Day 42	LS Mean (SE)	1.80 (0.04)	2.30 (0.04)	-0.50 (0.05)	<.0001
	95% CI	(1.73, 1.87)	(2.23, 2.37)	(-0.60, -0.40)	
Reduction from Baseline	LS Mean (SE)	1.11 (0.04)	0.60 (0.04)	0.50 (0.05)	<.0001
	95% CI	(1.03, 1.18)	(0.53, 0.67)	(0.40, 0.60)	
Percent Reduction from Baseline	LS Mean (SE)	37.58 (1.26)	20.70 (1.26)	16.88 (1.78)	<.0001
	95% CI	(35.10, 40.05)	(18.22, 23.17)	(13.38, 20.38)	
MPI PRFB[a]>=20%	n(Prop)	124 (87.3%)	61 (43.0%)		
	95% CI	(80.7%, 92.3%)	(34.7%, 51.5%)		

[a] PRFB = Percent Reduction from Baseline

The LSM for the difference in Overall MPI score between the two treatment groups at Day 14 was 0.59 (0.49, 0.69) and 20.40% (16.88%, 23.91%) for reduction and percent reduction, respectively. Similarly, for Day 42, the LSM for the difference in Overall MPI score between the two treatment groups was 0.50 (0.40, 0.60) and 16.88% (13.38%, 20.38%) for reduction and percent reduction, respectively. For both time points, the lower limit 95% CI for the difference was greater than the pre-defined non-inferiority margin (*i.e.*, -0.10 or -5%), therefore SPC was declared non-inferior to the OCA. In addition, since the 95% for the difference did not include zero, SPC was declared superior to OCA in the reduction of plaque (p-values of < 0.0001 for both time points).

For the proportion analysis, at Day 14 the proportion of subjects with reduction in MPI ≥ 20% was 87.3% (80.7%, 92.3%) for SPC and 41.5% (33.3%, 50.1%) for OCA. At Day 42, these outcomes were 87.3% (80.7%, 92.3%) for SPC and 43.0% (34.7%, 51.5%) for OCA.

Safety

There were eight adverse events reported in the study. Six of these were assessed as mild and two were reported as moderate in severity. Among the eight total events, three occurred in the SPC group and the remaining five were reported in the OCA group. All events were indicated as recovered/resolved upon study completion.

Discussion and Conclusions

The primary aim of this study was to compare the effect of the Philips Sonicare DiamondClean with Premium plaque control brush head to the Oral-B 7000 with CrossAction brush head on the reduction of gingival inflammation, per MGI, following a 42-day period of home use. The results show that the Sonicare power toothbrush performed significantly better than the Oral-B power toothbrush in this regard. Additionally, the Sonicare power toothbrush was similarly superior in all other endpoints of interest; namely, the reduction of gingival bleeding (GBI) and supragingival plaque (MPI). It is noted that significant differences were observed at both time points, Day 14 and Day 42, for all efficacy metrics.

With a reported eight adverse events out of 284 subjects over the 42-day study period, clinical review concludes that both products are safe for use in this population of subjects with moderate gingivitis.

The outcome in favor of the Sonicare power toothbrush is attributed to the high-frequency Sonicare drive train coupled with the novel Premium plaque control brush head design tested here. The brush head of this product was designed with bristle tufts embedded in a thermoplastic elastomer. Lacking the rigidity of hard plastic, the elastomer enables independent movement of each bristle tuft. The effect is that the brush head is optimized to conform to oral anatomy of varying types. For example, if a user has complex or malposed dentition that entraps bristles, thereby inhibiting bristle movement, the adjacent tufts of the Premium plaque control brush head are not affected and continue to sweep. The benefit of this functional operation is that, as the burden of plaque accumulation, even in complex areas, is diminished, the environment of the associated biofilm matrix is affected as a result, thus helping patients restore and preserve the health of the surrounding periodontium.

For both power toothbrushes tested in this study, there are marked changes in all efficacy endpoints as early as Day 14, emphasizing the transitional nature of gingivitis and the clinical benefits that can be

readily achieved in the home care setting when patients adopt a power toothbrush into their regime. This corroborates a recent consensus review for the implementation of power tooth brushing where plaque control is necessary to aid in the management of gingivitis and prevent progression to periodontitis.[23]

It is noted in this study, however, that the magnitude of the difference between products in all clinical endpoints consistently favors the Sonicare power toothbrush, importantly bringing this population of subjects exhibiting gingivitis back to a state where the hallmarks of inflammation, inflamed and bleeding tissue, are substantially diminished. The impact of this difference is also apparent in the proportion analysis, in which greater numbers of study participants in the Sonicare group were shown to benefit by a margin of 20% or more for all efficacy metrics evaluated.

This study represents a key benchmark in the success of this innovative power toothbrush. It was previously demonstrated to be superior to a manual toothbrush,[24] a minimum requirement of release of the product. In directly comparing to Oral-B 7000 with CrossAction brush head and SmartGuide accessory, the results here distinguish the Philips Sonicare DiamondClean with Premium plaque control brush head from the premium segment of marketed power toothbrushes in its ability to demonstrably reduce gingival inflammation, gingival bleeding, and plaque. Indeed, statistically significant differences between products were apparent within 14 days of use, and were, importantly, sustained to the terminus of the study at Day 42.

Acknowledgment: This study was sponsored by Philips Oral Healthcare.

Conflict of Interest: Source for funding: MS, MD, MW, and SS are employees of Philips, maker of the Sonicare powered toothbrush that was tested in this study. KM and JM are employees of an independent clinical research site.

For correspondence with the authors of this paper, contact Michelle Starke – michelle.starke@philips.com.

References

1. Korman KS. Mapping the pathogenesis of periodontitis: a new look. *J Periodontol* 2008;79(8 Suppl):1560-8.
2. Löe H, Theilade E, Jensen SB. Experimental gingivitis in man. *J Periodontol* 1965;36:177-87.
3. Marsh PD. Dental plaque as a microbial biofilm. *Caries Res* 2004;38:204-11.
4. Hall-Stoodley L, Costerton JW, Stoodley P. Bacterial biofilms: from the natural environment to infectious diseases. *Nat Rev Microbiol* 2004;2:95-108.
5. Socransky SS, Haffajee AD. Periodontal microbial ecology. *Periodontol 2000* 2005;38:135-87.
6. Socransky SS, Haffajee AD, Cugini MA, Smith C, Kent RL. Microbial complexes in subgingival plaque. *J Clin Periodontol* 1998;25:134-44.
7. Tanner A, Maiden MF, Maucuch PJ, Murray LL, Kent RL. Microbiota of health, gingivitis and initial periodontitis. *J Clin Periodontol* 1998;25:85-98.
8. Thomas JG, Nakaishi LA. Managing the complexity of a dynamic biofilm. *J Am Dent Assoc* 2006;137(11 supplement):10S–5.
9. Kumar PS, Leys EJ, Bryk JM, Martinez FJ, Moeschberger ML, Griffen AL. Changes in periodontal health status are associated with bacterial community shifts as assessed by quantitative 16S cloning and sequencing. *J Clin Microbiol* 2006;44:3665-73
10. Yaacob M, Worthington H, Deacon S, Deery C, Walmsley A, Robinson P, Glenny A. Powered versus manual toothbrush for oral health (review). *Cochrane Database of Systematic Reviews* 17, CD002281.
11. Offenbacher S, Barros S, Mendoza L, Preisser J, Moss K, De Jager M, Aspiras M. Changes in gingival crevicular fluid inflammatory mediator levels during the induction and resolution of experimental gingivitis in humans. *J Clin Periodontol* 2010;37:324-33
12. Holt J, Sturm D, Master A, Jenkins W, Schmitt P, Hefti A. A randomized, parallel-design study to compare the effects of the Sonicare Flexcare and the Oral-B P40 manual toothbrush on plaque and gingivitis. *Compend Contin Educ Dent* 2007;28:35-41.
13. Moritis K, Delaurenti M, Johnson M, Berg J, Boghosian A. Comparison of the Sonicare Elite and a manual toothbrush in the evaluation of plaque reduction. *Am J Dent* 2002;15(Spec Iss): 23B-5.
14. Kugel G, Boghosian A. Impact of the Sonicare toothbrush on plaque and gingivitis. *Compend Contin Educ Dent* 2002;23:7-10.
15. Goyal CR, Quqish JG, Galustians J, Ortbald K. Efficacy and safety of a new power toothbrush in a population with mild to moderate gingivitis. *J Clin Dent* 2007;18:65-9.
16. Klukowska M, Sharma NC, Grender J, Conde E, Cunningham P, Qaqish J. Comparative anti-gingivitis efficacy of oscillation-rotation electric toothbrush vs. manual toothbrush. *J Dent Res* 2014;93(Spec Iss A): Abs 1366.
17. Lobene R, Weatherford T, Ross NM, Lamm RA, Menaker L. A modified gingival index for use in clinical trials. *Clin Prev Dent* 1986;8:3-6.
18. Van der Weijden F, Timmerman MF, Nijboer A, Reijerse E, Van der Velden U. Comparison of different approaches to assess bleeding on probing as indicators of gingivitis. *J Clin Periodontol* 1994;21:589-94.
19. Lobene R, Soparkar P, Newman M. (1982). Use of dental floss, effect on plaque and gingivitis. *Clin Prev Dent;*4:5-8.
20. Quigley GA, Hein JW. Comparative cleansing efficiency of manual and power brushing. *J Am Dent Assoc* 1962;65:26-9.
21. Chow S-C, Liu J-P. (2004) Equivalence and noninferiority trials. In: *Design and Analysis of Clinical Trials, Concepts and Methodologies, Second Edition*. Hoboken, NJ, John Wiley & Sons, Inc., pp. 481-92.
22. US Department of Health and Human Services. (2016) Non-inferiority trials to establish effectiveness, guidance for industry. Available from: http://www.fda.gov/downloads/Drugs/Guidances/UCM202140.pdf [accessed Jan 2017].
23. Chapple ILC, Van der Weijden F, Doerfer C, Herrera D, Shapira L, Polak D, Madianos P, Louropoulou A, Machtei E, Donos N, Greenwell H, Van Winkelhoff AJ, Eren Kuru B, Arweiler N, Teughels W, Aimetti M, Molina A, Montero E, Graziani F. Primary prevention of periodontitis: managing gingivitis. *J Clin Periodontol* 2015;42(*Suppl* 16):S71-6.
24. Jenkins W, Souza S, Ward M, Defenbaugh J, Milleman K, Milleman J. An evaluation of plaque and gingivitis reduction following home use of Sonicare Flexcare Platinum with Premium plaque control brush head and a manual toothbrush. *J Clin Dent* 2017;28(Spec Iss A):A7-12).

Gingival Health and Plaque Regrowth Response Following a Four-Week Interdental Hygiene Intervention

Anthony Mwatha, MS, BSc Misty Olson, BA Sonia Souza, PhD Marilyn Ward, DDS Wendy Jenkins, BA

Philips Healthcare
Bothell, WA, USA

Pejmon Amini, DDS, MS John Gallob, DMD, BSN Theresa Fafard

Silverstone Research Group
Las Vegas, NV, USA

Abstract

- **Objectives:** To compare the efficacy of three adjunct interproximal cleaning methods versus a manual toothbrush alone on gingivitis, and demonstrate that the Philips Sonicare AirflossPro™ interproximal (IP) cleaning device provides a similar reduction in gingivitis and plaque compared to string floss.
- **Methods:** A randomized, single-blind, parallel-design study was conducted on generally healthy adults exhibiting mild to moderate gingivitis. Eligible subjects were non-smokers, aged 18–65 years, with ≥ 0.5 per the Rustogi Modified Navy Plaque Index (RMNPI) and a Gingival Bleeding Index (GBI) of ≥ 1 on at least 10 sites. Eligible subjects were randomly assigned to use one of four oral hygiene regimens: manual toothbrush (MTB) alone; MTB plus string floss (SF); MTB plus Philips Sonicare AirflossPro used with Cool Mint Listerine® Antiseptic (AFPL); and MTB plus Philips Sonicare AirflossPro used with BreathRx™ (AFPB). Subjects were followed over a 28-day home-use period, with follow-up visits for efficacy and safety conducted at Days 14 and 28. All subjects were instructed to use the MTB twice daily and perform interproximal cleaning once daily, if assigned. Study efficacy endpoints included the Modified Gingival Index (MGI), Rustogi Modified Navy Plaque Index, and the Gingival Bleeding Index.
- **Results:** Of 290 randomized subjects, 287 were followed to Day 14 and 286 were followed to Day 28. For the primary endpoint at Day 14, significantly larger reductions in MGI were observed in each of the three IP cleaning groups compared to MTB alone ($p < 0.001$). The adjusted mean reductions and standard error estimates (SE) for MGI expressed as a percent reduction from Baseline at Day 14 were: 0.22% (0.55%) for MTB; 4.30% (0.44%) for SF; 4.55% (0.45%) for AFPL; and 4.20% (0.44%) for AFPB. A non-inferiority test comparing AirflossPro to SF showed AirflossPro to be non-inferior to SF ($p < 0.001$).
- **Conclusions:** The addition of interproximal cleaning to manual tooth brushing statistically significantly reduces gingivitis and plaque compared to manual tooth brushing alone. Among the adjunct interproximal cleaning regimens, AirflossPro provides a similar reduction in gingivitis and plaque to string floss. All study regimens were safe on oral tissues.

(J Clin Dent 2017;28(Spec Iss A):A36–44)

Introduction

According to research conducted by the Centers for Disease Control and Prevention (CDC), one out of every two Americans over age 30 has some form of periodontal disease.[1] This finding is based on data collected as part of the CDC's 2009–2010 National Health and Nutrition Examination Survey (NHANES), designed to assess the health and nutritional status of adults and children in the United States. The 2009–2010 NHANES included for the first time a full-mouth periodontal examination to assess for mild, moderate, or severe periodontitis, making it the most comprehensive survey of periodontal health ever conducted in the United States. Researchers measured periodontitis because it is the most destructive form of periodontal disease. In an update of this study published in 2015, the authors suggested that prevalence might be even higher when including gingivitis in the spectrum of periodontal diseases.[2]

The progression from a state of oral health to disease passes through this transient state of gingivitis, where gingival inflammation and bleeding is reversible when adequately treated. An important part of this treatment is daily intervention by the patient in his/her home-care routine.

Across the organizations of the American Dental Association,[3] the United States Department of Disease Prevention and Health Promotion,[4] the American Academy of Periodontology,[5] and the European Federation of Periodontology[6] there is a consistent recommendation that a patient's home-care routine include daily tooth brushing and interproximal cleaning to mechanically remove plaque on all tooth surfaces. Interproximal cleaning is a critical part of maintaining periodontal health as the interdental space is susceptible to plaque and food accumulation that cannot be removed with tooth brushing alone.[7-9] As infection often initiates and progresses from the tissues immediately adjacent to interproximal tooth sites, it is incumbent upon the dental professional to advocate and educate patients on the importance of adopting regular interdental cleaning into their home-care regime. Yet, in spite of doing so, interproximal cleaning continues to be a difficult challenge for patients to habitually adopt.

Patient compliance with regular and sustained use of string floss as an interdental cleaning method has been difficult to determine, with reports indicating daily habitual use as low as 2%.[10] Furthermore, a recent Harris poll conducted of behalf of the American Academy of

Periodontology showed that more than one-quarter of Americans lie to their dentists about flossing habits, and 36% reported they would rather do an unpleasant activity, like working on taxes, than flossing.[11] This has been reaffirmed in consumer-based online blogs,[12] prompting the question, "If the use of string floss is so low and yet important to oral health, is there a better way for patients to clean interproximally that is as effective as string floss in promoting oral health, but experientially more pleasant to habitually perform?"

The Philips Sonicare AirflossPro™ device (Philips, Bothell, WA, USA) was developed as just such an alternative. It is a hand-held, powered, rechargeable device fitted with an angled tip that a patient can easily maneuver and place at each interproximal site. When actuated by a simple button press, the AirflossPro device emits a microburst of high velocity air and liquid micro-droplets (averaging between 35–45 m/s) through the angled tip. The droplets travel with sufficient shearing force (maximum shear stresses of up to 1300 Pa) to remove plaque biofilm from interproximal tooth surfaces. Consistent with its Philips Sonicare power toothbrush heritage, the device was designed to fit ergonomically in the hand, be safe on oral tissues, and easy to use, thus to help patients adopt daily habitual use where past attempts to regularly use string floss have fallen short.

As part of the development of the AirflossPro, users commented that the experience was enhanced even further when mouthrinse was used in the fluid reservoir in place of water. It is noted that AirflossPro is not an oral irrigator. The required amount of fluid to fill the AirflossPro reservoir is 15 ml, as opposed to 600 ml required for oral irrigators. Further, the mechanism of action is entirely different between the two technologies. Whereas AirflossPro shears away plaque biofilm by projecting low-volume, high velocity air and water droplets through the interproximal space, oral irrigators saturate oral tissues and biofilm with high volumes of fluid at low velocity.

The intent of the current study was to confirm, in a prospective, randomized, controlled clinical trial, that AirflossPro, when used with mouthrinse, met the specified efficacy target of imparting greater plaque removal and gingival health benefits than tooth brushing alone, and also to establish its efficacy as non-inferior to the standard for interproximal cleaning, string floss. Of further interest was the intent to confirm the efficacy of the device when used with mouthrinse in lieu of water. As a result, two mouthrinse formulations are included; the first, BreathRx™ (Philips, Bothell, WA, USA), is an essential oil-based rinse that contains zinc gluconate and cetylpyridinium chloride (CPC) as its active ingredient; the second, Listerine® Cool Mint Antiseptic (Johnson & Johnson, New Brunswick, NJ, USA), contains essential oils as the active ingredient. Note that the statistical design of the study was not intended to show a difference in efficacy between rinse formulations when used with AirflossPro, it was only to establish that either rinse, with their different active ingredients, is effective, thus giving patients confidence to choose based on preference.

Materials and Methods

Study Design and Objectives

This was a prospective, examiner-blind, parallel study designed to compare the capability of three interproximal cleaning devices to the ADA reference manual toothbrush (MTB) in reducing gingivitis and plaque. Data were collected at three study visits: Baseline (Visit 1), Day 14 ± 2 days (Visit 2), and Day 28 ± 2 days (Visit 3). Subjects observed a two- to six-hour plaque accumulation period prior to all study visits. Figure 1 depicts the study procedures by visit.

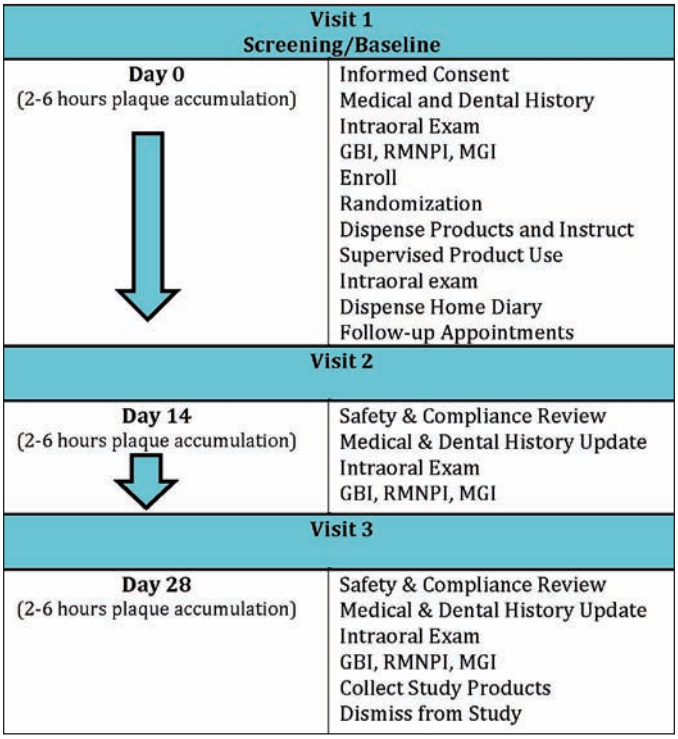

Figure 1. S*tudy procedures and visit flow.*

The primary objective of the study was to demonstrate the superiority of the interproximal cleaning regimens to manual tooth brushing alone in reducing gingival inflammation, and to establish statistical non-inferiority of the same among the interproximal regimens following a 14-day period of home use.

Secondary objectives of the study included similar superiority efficacy targets for plaque and gingival bleeding reduction between IP regimens and MTB alone, following 14 and 28 days of home use. Establishing the safety of the study products was also a secondary objective.

This study was reviewed and approved by the U.S. Investigational Review Board (IRB) and is registered on Clinicaltrials.gov (NCT02187016).

Efficacy and Safety Measurements

Efficacy was evaluated by examiners trained in the visual assessment of plaque, gingival bleeding, and gingival inflammation per accepted and standard visual clinical metrics. The efficacy examiners were blinded to the treatment allocation of the study subjects in order to minimize bias. In this study, the following measurements were utilized: the Modified Gingival Index[13] (MGI); the Rustogi Modified Navy Plaque Index[14] (RMNPI); and the Gingival Bleeding Index[15] (GBI). Table I shows the scale and description of the associated scores, per Index.

Safety was assessed via examination of the oral cavity to note evidence of gingival abrasion, irritations, lacerations, or ulcerations. Notations were made of any Baseline anomalies present on oral tissues, and at subsequent visits a repeat oral examination was performed to document any adverse changes in the oral cavity over the preceding period. Any incidents noted on a subject's home diary card were also evaluated and included in the study record as an Adverse Event, as appropriate.

Table I
Scoring Methodology for Efficacy Metrics; Plaque, Gingival Inflammation and Gingival Bleeding

Rustogi Modification of the Navy Plaque Index; 18 sites per tooth excluding 3rd molars				
0	1	N/A	N/A	N/A
No plaque	Plaque Present			
Modified Gingival Index, 2 sites per tooth excluding 3rd molars				
0	1	2	3	4
Absence of inflammation	Mild inflammation, slight change in color, little change in texture of any portion of but not the entire margin or papillary gingival unit	Mild inflammation but involving the entire margin or papillary unit	Moderate inflammation; glazing, redness, edema and/or hypertrophy of margin or papillary unit	Severe inflammation; marked redness, edema and/or hypertrophy or marginal or papillary gingival unit, spontaneous bleeding, congestion or ulceration
Gingival Bleeding Index, 2 sites per tooth excluding 3rd molars				
0	1	2	3	N/A
No bleeding	Bleeding on gently probing	Bleeding appears immediately upon gently probing	Spontaneous bleeding which is present prior to probing	

Subjects

Eligible subjects were able to provide Informed Consent, were non-smokers, aged 18–65 years, who were routine manual toothbrush users and who used string floss (or any other interproximal cleaning technique) once per week or less often. Enrolled participants had a minimum average plaque score of ≥ 0.5 per RMNPI following a two- to six-hour plaque accumulation, and a minimum of 10 sites with a score of ≥ 1 per GBI, thus to recruit a population with mild to moderate gingivitis. Subjects with insulin-dependent diabetes, advanced periodontal disease or excessive gingival recession, a diagnosis of xerostomia, or rampant decay were excluded from the study. None of the subjects were routine power toothbrush users, currently using professionally dispensed bleaching products, had orthodontic bands interfering with efficacy outcomes, had extensive crown and bridge work, or had a professional prophylaxis within four weeks of the study.

Study Treatment Groups

There were four treatment groups evaluated in this study. Common to all treatment groups was the use of an American Dental Association (ADA) reference manual toothbrush. It was to be used twice daily with fluoride-containing Crest® Cool Mint Gel dentifrice (Procter & Gamble, Cincinnati, OH, USA) for a one-minute brushing encounter per episode. For subjects randomized to the control MTB group, this was their only home oral hygiene procedure. The remaining subjects were randomized to one of three adjunct IP cleaning regimens: string floss (Reach® Unflavored Waxed Floss, Johnson & Johnson, New Brunswick, NJ, USA), AirflossPro used with BreathRx mouthrinse (AFPB), or AirflossPro used with Listerine Cool Mint Antiseptic mouthrinse (AFPL).

All groups were instructed on product use by designated study personnel, with subjects demonstrating understanding of the directions by using their assigned study products in the presence of the assigned instructor. Step-by-step illustrated instructions were also provided for home reference, as was a diary card for subjects to keep a record of product use.

Randomization and Data Capture

Subjects who met the eligibility criteria were enrolled and then randomized to one of the four study treatment groups for the 28-day home-use period. Randomization was stratified by gender so that the number of males and females was balanced across the treatment groups.

Study data were collected on a web-based Electronic Data Capture System. Access to the web-based system was limited by log-in credentials that matched the study role of the user. Applicable source document forms were utilized where necessary. Study data were monitored to ensure accuracy of the data set prior to any analysis. The randomization assignment of subjects was merged with the randomization schedule following cleaning and final locking of the study database.

Statistical Methods

Sample Size Determination. Based on previous studies, a difference of 0.2 units, with standard deviation (SD) equal to 0.3 in MGI reduction, or 20% (SD = 22%) reduction in MGI between any of the IP treatments and MTB alone were considered to be clinically meaningful. With this premise, a sample size of 275 subjects (50 in the MTB only group and 75 in each of the three IP groups) would allow for greater than 80% power to detect this difference in MGI between any one of three IP groups, and the MTB-alone group, using a two-sided t-test with a 0.05 significance level. Also, to demonstrate non-inferiority between AirflossPro and the SF group, a sample size of 225 subjects (150 subjects in the AirflossPro group and 75 in the SF group) would provide approximately 80% power for a one-sided 0.025 test with a non-inferiority margin of approximately 60% between the SF and MTB alone, and assuming a true mean difference between the two groups was zero with standard deviations of 0.3. To account for loss to follow-up, estimated to be 10%, approximately 308 subjects were to be randomized (56 subjects for MTB alone and 84 for each of the other three groups) in order to complete with the required number of subjects.

Efficacy Endpoints. Efficacy endpoints, MGI, GBI, and MPI, were scored at the tooth sites prescribed for each Index using the scoring methodology described in Table I. A standardized case report form was used to record these data at each study visit. For each Index and for each subject three summary efficacy variables were defined. These included: an overall Index score calculated as the sum of scores of all evaluable sites divided by the number of evaluable sites; reduction from Baseline, calculated as the Baseline score minus the post-Baseline score; and percent reduction from Baseline, calculated as the reduction in score divided by the Baseline score times 100. All three summary scores were calculated for the whole mouth and for sub- regions of the mouth, and were considered as continuous variables.

All variables were summarized using descriptive statistics, including means, medians, standard deviations, and ranges for continuous variables, and number and percent for categorical variables. All analyses were conducted using SAS® software.

Primary Efficacy Analysis. The primary efficacy analysis was performed on the modified intent to treat (mITT) population that was defined to include randomized subjects with a Baseline and a Day 14 MGI score. An analysis of variance model (ANOVA), with the Baseline MGI and randomization group as predictors, was used to estimate the Day 14 adjusted mean MGI score. Two similar models were also used to estimate adjusted mean reduction in MGI score and adjusted mean percent reduction in MGI score. Since multiple comparisons (MTB group versus each of the IP groups) were to be performed, if the overall null hypothesis of no difference between the four groups was rejected, 95% confidence intervals (CI) and p-values were adjusted using the procedure described by Dunnett.[16]

If the superiority of the interproximal treatment groups versus the manual tooth brushing group was established, the effect of AirflossPro versus SF was to be evaluated using a non-inferiority analysis. To formally evaluate the non-inferiority of AirflossPro to SF, the AFPL and AFPB groups were to be compared. If no statistically significant difference in these two groups was observed, they would be combined into one group. Otherwise, two separate non-inferiority tests of the AFPL and AFPB versus SF were to be performed.

For non-inferiority, the following hypothesis, to demonstrate that AirflossPro preserved at least 60% of the effect of SF, was to be evaluated:

$$H_0: \mu_{AIRFLOSS} - \mu_{SF} \leq -\ \delta\ (\mu_{SF} - \mu_{MTB})$$

$$H_A: \mu_{AIRFLOSS} - \mu_{SF} > -\ \delta\ (\mu_{SF} - \mu_{MTB})$$

Where $\mu_{SF} - \mu_{MTB}$ represents the efficacy of the active control (SF) over MTB alone, $\mu_{AIRFLOSS} - \mu_{SF}$ represents the difference in efficacy between AirflossPro and SF, and δ (= 60%) represents an acceptable preservation fraction. Using the approach described by Pigeot, *et al*.,[17] non-inferiority was to be evaluated via a contrast test for the parameter:

$$\psi(\hat{\mu}) = \hat{\mu}_{AIRFLOSS} - (1-\delta)\ \hat{\mu}_{SF} - \hat{\mu}_{MTB}$$

which represents a reformulated linear contrast of the hypothesis to be tested, where, $\mu_{AIRFLOSS}$ μ_{SF} and μ_{MTB} represent the estimated means for AirflossPro, string floss, and MTB groups, respectively. AirflossPro would be declared as non-inferior to the SF regimen if this contrast was found to be statistically significantly different from zero.

Secondary Efficacy and Safety Analysis. Secondary objectives compared the IP cleaning devices to MTB for plaque (RMNPI) and gingival bleeding (GBI) outcomes at Days 14 and 28. In addition, non-inferiority in gingivitis reduction for AirflossPro compared to SF at Day 28, and for plaque reduction (RMNPI) at Days 14 and 28 were evaluated. The secondary analyses included all randomized subjects with a Baseline and a post-Baseline evaluation for the parameter and time point of interest. A statistical model similar to the primary analysis was to be used to estimate adjusted means, SEs of the means, and two-sided 95% CI.

The analysis of safety included all randomized subjects exposed to any of the four regimens.

Results

Demographics

Two-hundred ninety-three subjects provided informed consent and were screened for study participation. Of these, 290 were enrolled and randomized with 287 subjects completing the Day 14 visit (mITT population) and 286 completing the Day 28 visit. Of the three randomized subjects excluded from the mITT population, two were lost to follow-up and one chose to discontinue due to a conflict in the subject's schedule. The one additional subject who did not complete the Day 28 visit was lost to follow-up. Table II provides a summary of demographic characteristics for randomized subjects. There were no significant differences in the age and gender distribution among the four study groups, indicating comparable groups at Baseline. The overall mean age of randomized subjects was 35.6 years, with 64% females.

Primary Efficacy Results

Modified Gingival Index. Since the primary and secondary efficacy measures evaluated the same outcome (MGI) but at different time points, results of the primary and secondary efficacy analysis for MGI are presented together in this section.

At Baseline, the mean MGI scores among the 290 randomized subjects did not differ statistically significantly between the four groups ($p = 0.654$). The mean scores were 2.25 (SD = 0.13) for the MTB group, 2.25 (SD = 0.14) for SF, 2.25 (SD = 0.13) for AFPL, and 2.27 (SD = 0.14) for AFPB.

Table III presents model-based estimates for the mean MGI score at Baseline, Day 14, and Day 28, and mean MGI percent reduction from Baseline for the four study groups.

Following 14 days of use, the adjusted mean (95% CI) MGI scores were 2.25 (2.22, 2.27) for MTB, 2.15 (2.13, 2.17) for SF, 2.15 (2.13, 2.17) for AFPL, and 2.16 (2.14, 2.18) for AFPB.

Following 28 days of use, the adjusted mean (95% CI) MGI scores were 2.23 (2.20, 2.26) for MTB, 2.00 (1.97, 2.02) for SF, 2.04 (2.01, 2.06) for AFPL, and 2.06 (2.03, 2.08) for AFPB. A boxplot of percent reduction from Baseline for the four study groups for MGI is presented in Figure 2.

All three IP devices were significantly better than MTB in reducing gingivitis for the whole mouth at both time points ($p < 0.001$). At both visits (Days 14 and 28) the contrast test for inferiority was rejected ($p < 0.001$). That is, the AirflossPro device (AFPL and AFPB combined)

Table II
Demographic Characteristics

Parameter	Category	Treatment				Total	p-value
		MTB	Floss	AFP + Listerine	AFP + Breath Rx		
Age (yrs)	No. Subjects	51	79	80	80	290	
	Mean(SD)	35.1 (12.10)	34.9 (11.00)	35.2 (10.90)	36.9 (12.10)	35.6 (11.50)	0.835
	Median	32	32	33	34	33	
	Min, Max	(19, 65)	(18, 62)	(18, 57)	(19, 61)	(18, 65)	
Gender	Female	33 (64.7%)	51 (64.6%)	51 (63.8%)	51 (63.8%)	186 (64.1%)	0.999
	Male	18 (35.3%)	28 (35.4%)	29 (36.3%)	29 (36.3%)	104 (35.9%)	

Table III
Modified Gingival Index, Adjusted Means, at Baseline, Day 14, Day 28

Variable	Statistic	Treatment				p-value[a]
		MTB	Floss	AFP + Listerine	AFP + Breath Rx	
Baseline	No Subjects	51	79	78	79	
	Mean (SE)	2.25 (0.02)	2.25 (0.02)	2.24 (0.02)	2.27 (0.02)	0.420
	95% CI	(2.21, 2.28)	(2.22, 2.28)	(2.21, 2.27)	(2.24, 2.30)	
	Diff[b] Mean (SE)		0.00 (0.02)	-0.00 (0.02)	0.03 (0.02)	
	Diff 95% CI		(-0.05, 0.06)	(-0.06, 0.05)	(-0.03, 0.09)	
	Diff p-value[c]		1.000	0.999	0.446	
Day 14 Post-treatment						
	Adjusted Mean (SE)	2.25 (0.01)	2.15 (0.01)	2.15 (0.01)	2.16 (0.01)	< 0.001
	95% CI	(2.22, 2.27)	(2.13, 2.17)	(2.13, 2.17)	(2.14, 2.18)	
	Diff[b] Mean (SE)		-0.09 (0.02)	-0.10 (0.02)	-0.09 (0.02)	
	Diff 95% CI		(-0.13, -0.06)	(-0.13, -0.06)	(-0.13, -0.05)	
	Diff p-value[c]		< 0.001	< 0.001	< 0.001	
% Reduction						
	Adjusted Mean (SE)	0.22 (0.55)	4.30 (0.44)	4.55 (0.45)	4.20 (0.44)	< 0.001
	95% CI	(-0.87, 1.30)	(3.42, 5.17)	(3.67, 5.42)	(3.32, 5.07)	
	Diff[b] Mean (SE)		4.08 (0.71)	4.33 (0.71)	3.98 (0.71)	
	Diff 95% CI		(2.43, 5.73)	(2.68, 5.99)	(2.32, 5.64)	
	Diff p-value[c]		< 0.001	< 0.001	< 0.001	
Day 28 Post-treatment	No Subjects	51	78	78	79	
	Adjusted Mean (SE)	2.23 (0.02)	2.00 (0.01)	2.04 (0.01)	2.06 (0.01)	< 0.001
	95% CI	(2.20, 2.26)	(1.97, 2.02)	(2.01, 2.06)	(2.03, 2.08)	
	Diff[b] Mean (SE)		-0.23 (0.02)	-0.19 (0.02)	-0.17 (0.02)	
	Diff 95% CI		(-0.28, -0.18)	(-0.24, -0.14)	(-0.22, -0.12)	
	Diff p-value[c]		< 0.001	< 0.001	< 0.001	
% Reduction						
	Adjusted Mean (SE)	1.10 (0.72)	11.41 (0.58)	9.54 (0.58)	8.52 (0.58)	< 0.001
	95% CI	(-0.31, 2.50)	(10.27, 12.55)	(8.40, 10.67)	(7.39, 9.65)	
	Diff[b] Mean (SE)		10.31 (0.92)	8.44 (0.92)	7.42 (0.92)	
	Diff 95% CI		(8.16, 12.46)	(6.29, 10.59)	(5.27, 9.57)	
	Diff p-value[c]		< 0.001	< 0.001	< 0.001	

Note: ANOVA Model is: Outcome = Treatment + Baseline Result + error.
[a] p-value is based on a fixed effects ANOVA model F-test (Ho: All treatments are equal).
[b] Diff Mean = Estimated Difference in the adjusted means, IP device minus MTB alone.
[c] Dunnets test. The treatment groups floss, Listerine and Breath Rx are compared to MTB.

preserved at least 60% of the efficacy between SF and MTB alone in reducing gingivitis based on MGI (Table VI).

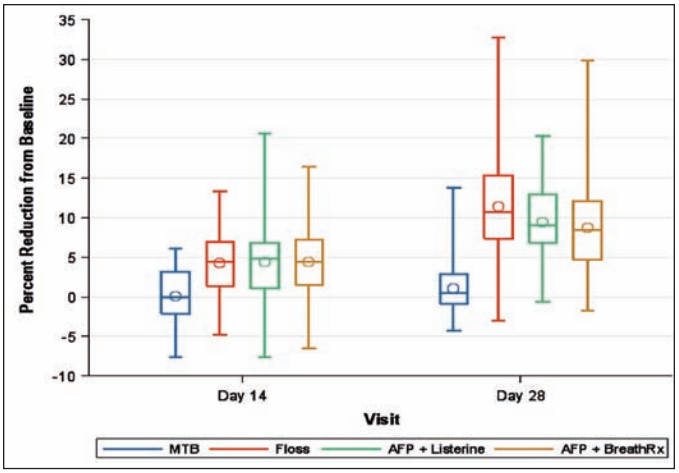

Figure 2. *Modified Gingival Index, percent reduction from baseline, overall.*

Secondary Efficacy Results

Gingival Bleeding Index. At Baseline, the mean GBI scores among the 290 randomized subjects did not differ significantly between the four groups (p = 0.509). The mean scores were 0.19 (SD = 0.08) units for the MTB group, 0.20 (SD = 0.07) for SF, 0.19 (SD = 0.08) for AFPL, and 0.21 (SD = 0.08) for AFPB.

Table IV presents model estimates for adjusted mean GBI scores for Baseline, Day 14, and Day 28, and adjusted mean GBI percent reduction from Baseline for the four study groups.

Following 14 days of use, the adjusted mean (95% CI) GBI scores for the four study groups were 0.19 (0.18, 0.20) for MTB, 0.15 (0.14, 0.16) for SF, 0.15 (0.14, 0.15) for AFPL, and 0.15 (0.14, 0.15) for AFPB.

At Day 28, the adjusted mean (95% CI) GBI scores were 0.19 (0.17, 0.20) for MTB, 0.11 (0.10, 0.12) for SF, 0.12 (0.11, 0.13) for AFPL, and 0.12 (0.11, 0.13) for AFPB. Figure 3 depicts these results for percent reduction from Baseline in a boxplot. Statistical superiority was observed between the IP cleaning regimens compared to manual tooth brushing alone; p-value < 0.001 at both Day 14 and Day 28.

Rustogi Modification of the Navy Plaque Index. The mean RMNPI scores among the 290 randomized subjects at baseline did not differ significantly between the four groups (p = 0.131). The mean scores were 0.66 (SD = 0.05) units for the MTB group, 0.63 (SD = 0.04) for SF, 0.64 (SD = 0.05) for AFPL. and 0.65 (SD = 0.05) for AFPB.

Table V presents model estimates for adjusted mean RMNPI scores for Baseline, Day 14, and Day 28, and adjusted mean RMNPI percent reduction from Baseline for the four study groups.

Following 14 days of use, the adjusted mean (95% CI) plaque scores were 0.61 (0.59, 0.62) for MTB, 0.53 (0.52, 0.54) for SF, 0.54 (0.53, 0.55) for AFPL, and 0.55 (0.54, 0.56) for AFPB.

Table IV
Gingival Bleeding Index, Adjusted Means, at Baseline, Day 14, Day 28

Variable	Statistic	Treatment				p-value[a]
		MTB	Floss	AFP + Listerine	AFP + Breath Rx	
Baseline	No Subjects	51	79	78	79	
	Mean (SE)	0.19 (0.01)	0.20 (0.01)	0.19 (0.01)	0.21 (0.01)	0.325
	95% CI	(0.17, 0.21)	(0.18, 0.22)	(0.17, 0.21)	(0.19, 0.23)	
	Diff[b] Mean (SE)		0.01 (0.01)	-0.01 (0.01)	0.02 (0.01)	
	Diff 95% CI		(-0.03, 0.04)	(-0.04, 0.03)	(-0.02, 0.05)	
	Diff[c] P-value		0.959	0.960	0.442	
Day 14 Post-treatment						
	Adjusted Mean (SE)	0.19 (0.006)	0.15 (0.005)	0.15 (0.005)	0.15 (0.005)	< 0.001
	95% CI	(0.18, 0.20)	(0.14, 0.16)	(0.14, 0.15)	(0.14, 0.15)	
	Diff[b] Mean (SE)		-0.04 (0.01)	-0.05 (0.01)	-0.05 (0.01)	
	Diff 95% CI		(-0.06, -0.03)	(-0.06, -0.03)	(-0.06, -0.03)	
	Diff P-value[c]		< 0.001	< 0.001	< 0.001	
% Reduction						
	Adjusted Mean (SE)	-0.16 (2.81)	22.89 (2.26)	26.90 (2.27)	24.61 (2.26)	< 0.001
	95% CI	(-5.69, 5.36)	(18.46, 27.33)	(22.42, 31.38)	(20.15, 29.06)	
	Diff[b] Mean (SE)		23.06 (3.60)	27.07 (3.61)	24.77 (3.61)	
	Diff 95% CI		(14.64, 31.48)	(18.62, 35.51)	(16.33, 33.21)	
	Diff P-value[c]		< 0.001	< 0.001	< 0.001	
Day 28 Post-treatment	No Subjects	51	78	78	79	
	Adjusted Mean (SE)	0.19 (0.006)	0.11 (0.005)	0.12 (0.005)	0.12 (0.005)	< 0.001
	95% CI	(0.17, 0.20)	(0.10, 0.12)	(0.11, 0.13)	(0.11, 0.13)	
	Diff[b] Mean (SE)		-0.08 (0.01)	-0.07 (0.01)	-0.07 (0.01)	
	Diff 95% CI		(-0.10, -0.06)	(-0.09, -0.05)	(-0.08, -0.05)	
	Diff P-value[c]		< 0.001	< 0.001	< 0.001	
% Reduction						
	Adjusted Mean (SE)	4.03 (2.85)	43.31 (2.30)	40.49 (2.31)	36.79 (2.30)	< 0.001
	95% CI	(-1.58, 9.64)	(38.78, 47.84)	(35.95, 45.03)	(32.28, 41.31)	
	Diff[b] Mean (SE)		39.28 (3.66)	36.46 (3.66)	32.76 (3.66)	
	Diff 95% CI		(30.72, 47.85)	(27.90, 45.03)	(24.20, 41.33)	
	Diff P-value[c]		< 0.001	< 0.001	< 0.001	

Note: ANOVA Model is: Outcome = Treatment + Baseline Result + error.
[a] p-value is based on a fixed effects ANOVA model F-test (Ho: All treatments are equal).
[b] Diff Mean = Estimated Difference in the adjusted means, IP device minus MTB alone.
[c] Dunnets test. The treatment groups floss, Listerine and Breath Rx are compared to MTB.

Following 28 days of use, the adjusted mean (95% CI) plaque scores were 0.61 (0.59, 0.62) for MTB, 0.47 (0.46, 0.48) for SF, 0.49 (0.48, 0.50) for AFPL, and 0.50 (0.49, 0.51) for AFPB. Figure 4 depicts these results for percent reduction from Baseline in a boxplot. Statistical superiority was observed between the adjunct interproximal cleaning regimens compared to manual tooth brushing alone; p-value < 0.001 at both Day 14 and Day 28. At both visits, the contrast test for inferiority was rejected (p < 0.001). That is, the AirflossPro device preserved at least 60% of the efficacy between SF and MTB alone in reducing plaque (Table VI).

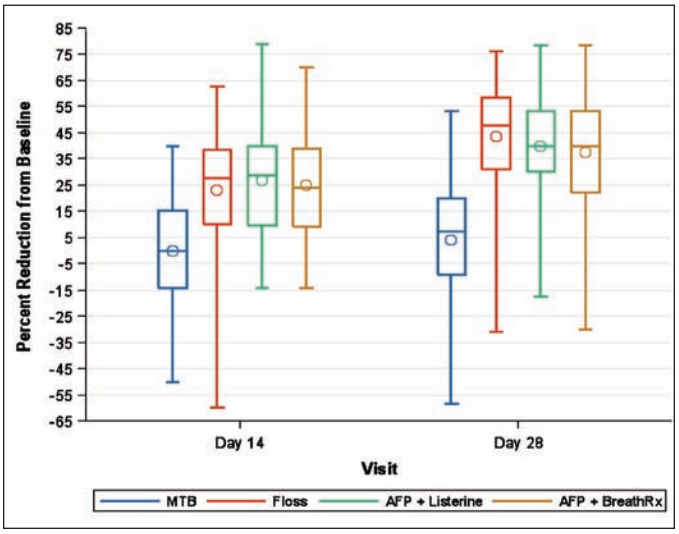

Figure 3. *Gingival Bleeding Index, percent reduction from baseline, overall.*

Safety

There were a total of four adverse events reported in the study. Two events occurred in two subjects randomized to AFPB, and one event each occurred in subjects randomized to SF and AFPL. Three of these events were reports of gingival irritation and one was a self-reported event of "gum irritation/soreness." All four events were characterized as mild in severity. The events were possibly related to the assigned study treatments. All four events were observed to resolution. There were no serious adverse events reported.

Discussion

The purpose of this study was to assess, in a controlled clinical trial, the extent to which the use of adjunct interproximal cleaning affected the status of gingival health and surface plaque in subjects with mild to moderate gingivitis, compared to manual tooth brushing alone. This study was successful in demonstrating that, indeed, daily interproximal cleaning can have a significant effect on these measures within just two weeks of use, persisting up to four weeks of use. Further, the regimens tested here are all safe for use.

Table V
Rustogi Modified Navy Plaque Index, Adjusted Means, at Baseline, Day 14, Day 28

Variable	Statistic	Treatment				p-value[a]
		MTB	Floss	AFP + Listerine	AFP + Breath Rx	
Baseline	No Subjects	51	79	78	79	
	Mean (SE)	0.66 (0.01)	0.63 (0.01)	0.64 (0.01)	0.65 (0.01)	0.046
	95% CI	(0.64, 0.67)	(0.62, 0.64)	(0.63, 0.65)	(0.64, 0.66)	
	Diff[b] Mean (SE)		-0.02 (0.01)	-0.02 (0.01)	-0.01 (0.01)	
	Diff 95% CI		(-0.04, -0.00)	(-0.04, 0.00)	(-0.03, 0.01)	
	Diff P-value[c]		0.020	0.098	0.454	
Day 14 Post-treatment						
	Adjusted Mean (SE)	0.61 (0.01)	0.53 (0.01)	0.54 (0.01)	0.55 (0.01)	< 0.001
	95% CI	(0.59, 0.62)	(0.52, 0.54)	(0.53, 0.55)	(0.54, 0.56)	
	Diff[b] Mean (SE)		-0.07 (0.01)	-0.07 (0.01)	-0.06 (0.01)	
	Diff 95% CI		(-0.09, -0.05)	(-0.09, -0.05)	(-0.08, -0.04)	
	Diff P-value[c]		< 0.001	< 0.001	< 0.001	
%Reduction						
	Adjusted Mean (SE)	5.56 (1.00)	17.07 (0.80)	15.95 (0.80)	14.33 (0.80)	< 0.001
	95% CI	(3.59, 7.52)	(15.50, 18.64)	(14.37, 17.53)	(12.76, 15.90)	
	Diff[b] Mean (SE)		11.51 (1.29)	10.39 (1.28)	8.77 (1.27)	
	Diff 95% CI		(8.51, 14.52)	(7.40, 13.39)	(5.80, 11.75)	
	Diff P-value[c]		< 0.001	< 0.001	< 0.001	
Day 28 Post-treatment	No Subjects	51	78	78	79	
	Adjusted Mean (SE)	0.61 (0.01)	0.47 (0.01)	0.49 (0.01)	0.50 (0.01)	< 0.001
	95% CI	(0.59, 0.62)	(0.46, 0.48)	(0.48, 0.50)	(0.49, 0.51)	
	Diff[b] Mean (SE)		-0.13 (0.01)	-0.12 (0.01)	-0.11 (0.01)	
	Diff 95% CI		(-0.15, -0.11)	(-0.14, -0.10)	(-0.13, -0.09)	
	Diff P-value[c]		< 0.001	< 0.001	< 0.001	
% Reduction						
	Adjusted Mean (SE)	5.70 (1.08)	26.48 (0.87)	23.96 (0.87)	22.41 (0.86)	< 0.001
	95% CI	(3.58, 7.83)	(24.76, 28.19)	(22.25, 25.66)	(20.72, 24.11)	
	Diff[b] Mean (SE)		20.77 (1.40)	18.25 (1.39)	16.71 (1.38)	
	Diff 95% CI		(17.51, 24.03)	(15.01, 21.50)	(13.49, 19.93)	
	Diff P-value[c]		< 0.001	< 0.001	< 0.001	

Note: ANOVA Model is: Outcome = Treatment + Baseline Result + error.
[a] p-value is based on a fixed effects ANOVA model F-test (Ho: All treatments are equal).
[b] Diff Mean = Estimated Difference in the adjusted means, IP device minus MTB alone.
[c] Dunnets test. The treatment groups floss, Listerine and Breath Rx are compared to MTB.

These outcomes corroborate the recommendation of the dental health community that interproximal cleaning is beneficial in helping to achieve and maintain the health of oral tissues.[3-6] The evidence here supports that interdental cleaning is effective in the transition state of mild to moderate gingivitis, where adequate intervention can bring patients back to health.

When interpreting the effects between the interproximal cleaning regimens tested in this study (string floss and AirflossPro), non-inferiority was achieved for the measures of MGI or RMNPI at both study time-points. This was an aim not only of this clinical trial, but also a key quality requirement of the AirflossPro device itself; it has no reason to be in patients' hands if it cannot clean as well as the dental professional standard, string floss. Indeed, in a population of users who have been unable to adopt a daily string flossing habit, AirflossPro is an effective alternative.

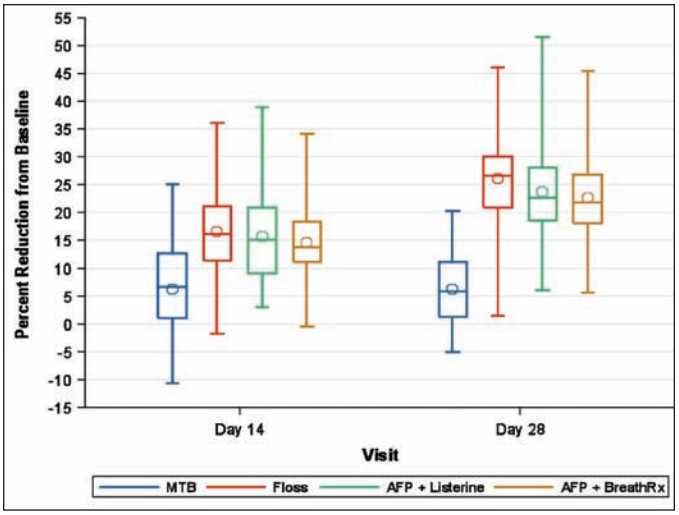

Figure 4. *Rustogi Modified Navy Plaque Index, percent reduction from baseline, overall.*

Airfloss has previously been demonstrated to be effective when used with water.[18] The selection and use of the antimicrobial rinses tested here was based on use-case scenarios, frequently described by patients who prefer the interproximal cleaning experience of Airfloss with rinse to that of water. The authors acknowledge that the antimicrobial agents contained in the rinse formulations were expected to aid in the benefits observed in the reduction of plaque and gingivitis in this study. Indeed, a recent consensus review emphasizes the evidence base for the adjunctive use of rinses that contain antiplaque agents as a means to help limit plaque regrowth and manage gingivitis.[19] However, the aim of this trial was not intended to show the extent to which the use of rinse contributes to the clinical benefits observed here, in comparison to water. Additional *in vivo* research is necessary to understand the short- and long-term benefits of a direct comparison.

The development of the AirflossPro device follows a trajectory that tracks scientific understanding and technological ideation,

Table VI
Non-inferiority Analysis, MGI, RMNPI

Variable	Statistic	Treatment MTB	Floss	AirflossPro
	No Subjects	51	78	157
MGI Reduction, Day 14				
	Adjusted Mean (95% CI)	0.01 (-0.02, 0.03)	0.10 (0.08, 0.12)	0.10 (0.09, 0.11)
	Diff Mean (95% CI)			0.06 (0.03, 0.08)
	Diff P-value[b]			< 0.001
MGI Reduction, Day 28				
	Adjusted Mean (95% CI)	0.03 (-0.00, 0.06)	0.26 (0.23, 0.28)	0.21 (0.19, 0.22)
	Diff Mean (95% CI)			0.09 (0.06, 0.11)
	Diff P-value[b]			< 0.001
RMNPI Reduction, Day 14				
	Adjusted Mean (95% CI)	0.04 (0.02, 0.05)	0.11 (0.10, 0.12)	0.10 (0.09, 0.11)
	Diff Mean (95% CI)			0.03 (0.02, 0.04)
	Diff P-value[b]			< 0.001
RMNPI Reduction, Day 28				
	Adjusted Mean (95% CI)	0.04 (0.02, 0.05)	0.17 (0.16, 0.18)	0.15 (0.14, 0.16)
	Diff Mean (95% CI)			0.06 (0.05, 0.07)
	Diff P-value[b]			< 0.001

[b] Diff Mean is defined as the estimated means for the contrast: AirflossPro - (0.4*Floss) - (0.6*MTB).

underpinned by the long-held insight that consumers and patients have a difficult time adopting string floss into their home oral hygiene regime because of its inherent difficulty and unpleasant experience. A treatment can only be as effective as the patient who adopts its usage. Thus, AirflossPro was developed as an option, in particular for patients who need the benefit of interproximal cleaning but who have never been able to effectively and habitually use string floss. Its hand-held form-factor, ergonomic handle design and angled tip have been designed around this user; buttons are placed where fingers naturally grip, the fluid requirements are negligible compared to oral irrigators, the nozzle features a soft-touch tip that can be gently guided across and positioned between teeth, and it has auto or manual modes for actuation of the plaque-shearing microburst spray of liquid and air. The use of a rinse in lieu of water can also enhance the overall user experience and, based on the outcomes reported here, it is both safe and effective to do so.

The current study only touched the surface of understanding the potential beneficial effects of the AirflossPro device on oral health. Here, its evaluation was limited to the clinical outcomes for which the device was originally intended; namely, as an easy-to-use way to shear off plaque biofilm from hard-to-reach interproximal tooth surfaces, thus help promote the health of adjacent gingival tissue. In theory, the AirflossPro device also potentially enables targeted delivery of health-promoting medicaments to sites where patients need them most, to those problematic interproximal contact sites along the gingivae. *In vitro* studies have shown that AirFlossPro not only removes bacterial biofilms, but also assists in deeper penetration of the antimicrobial chemistries found in mouthrinses compared to rinse alone.[20,21] Certainly, more clinical research is warranted to understand its effects in this broader conceptualization of how AirflossPro could be used as an aid in achieving and maintaining oral health.

Acknowledgment: This study was sponsored by Philips Oral Healthcare.

Conflict of Interest: Source for funding: AM, MO, SS, MW, and WJ are employees of Philips, maker of the Sonicare powered toothbrush that was tested in this study. PA, JG, and TF are employees of an independent clinical research site.

For correspondence with the authors of this paper, contact Wendy Jenkins – Wendy.Jenkins@philips.com

References

1. Eke PI, Dye BA, Wei L, Thornton-Evans GO, Genco RJ. Prevalence of periodontitis in adults in the United States: 2009 and 2010. *J Dent Res* 2012;91:914-20.
2. Eke PI, Dye BA, Wei L, Slade GD, Thornton-Evans GO, Borgnakke WS, Taylor GW, Page RC, Beck JD, Genco RJ. Update on prevalence of periodontitis in adults in the United States: NHANES 2009 to 2012. *J Periodontol* 2015;86:611-22.
3. American Dental Association. Available from: http://www.ada.org/en/press-room/news-releases/2016-archive/august/statement-from-the-american-dental-association-about-interdental-cleaners [accessed October 2016].
4. Office of Disease Prevention and Health Promotion. Available from: https://www.healthypeople.gov/2020/topics-objectives/topic/oral-health [accessed October 2016].
5. American Academy of Periodontology. Available from: https://www.perio.org/consumer/AAP-recommends-flossing-as-essential [accessed October 2016].
6. European Federation of Periodontology. Available from: http://www.efp.org/publications/EFP_Dossier_on_Periodontal_Disease.pdf [accessed October 2016].
7. Kinane DF. The role of interdental cleaning in effective plaque control: Need for interdental cleaning in primary and secondary prevention. In: *Proceedings of the European Workshop on Mechanical Plaque Control,* Lang NP, Löe H, Armstrong R, eds. Berlin, Quintessence, 156-68, 1998.
8. Löe H. Oral hygiene in the prevention of caries and periodontal disease. *Int Dent J* 2000;50:129-39.
9. Graves RC, Disney JA, Stamm JW. Comparative effectiveness of flossing and brushing in reducing interproximal bleeding. *J Periodontol* 1989;60:243-7.
10. Bader HI. Floss or die: implications for dental professionals. *Dent Today* 1998:17: 76-82.
11. Reuters U.S. Edition. Available from: http://www.reuters.com/article/2015/06/23/us-usa-healthcare-flossing-idUSKBN0P32BJ20150623 [accessed October 2016].
12. Thrillist. Available from: https://www.thrillist.com/health/nation/lying-to-your-dentist-about-flossing-do-dentists-know-you-lie-about-flossing?share=c [accessed October 2016].
13. Lobene RR, Weatherford T, Ross NM, Lamm RA, Menaker L. A modified gingival index for use in clinical trials. *Clin Prev Dent* 1986;8:3-6.
14. Rustogi KN, Curtis JP, Volpe AR, Kemp JH, McCool JJ, Korn LR. Refinement of the modified navy plaque index to increase plaque scoring efficiency in gumline and interproximal tooth areas. *J Clin Dent* 1992;3(Suppl C):C9-12.
15. Van der Weijden F, Timmerman M, Nijboer A, Reijerse E, Van der Velden U. Comparison of different approaches to assess bleeding on probing as indicators of gingivitis. *J Clin Periodontol* 1994;21:589-94.
16. Dunnett CW. A multiple comparison procedure for comparing several treatments

with a control. *J Am Stat Assoc* 1955;50:1096–121.
17. Pigeot I, Schäfer J, Röhmel J, Hauschke D. Assessing non-inferiority of a new treatment in a three-arm clinical trial including a placebo. *Stat Med* 2003;22:883–99.
18. De Jager M, Jain V, Schmitt P, DeLaurenti M, Jenkins W, Milleman J, Milleman K, Putt M. Effect of Sonicare AirFloss on interproximal plaque and gingivitis. *J Dent Res* 2011;90(Spec Iss A).
19. Chapple ILC, Van der Weijden F, Doerfer C, Herrera D, Shapira L, Polak D, Madianos P, Louropoulou A, Machtei E, Donos N, Greenwell H, Van Winkelhoff AJ, Eren Kuru B, Arweiler N, Teughels W, Aimetti M, Molina A, Montero E, Graziani F. Primary prevention of periodontitis: managing gingivitis. *J Clin Periodontol* 2015;42(Suppl 16):S71–6.
20. Fabbri S, Johnston DA, Rmaile A, Gottenbos B, De Jager M, Aspiras M, Starke EM, Ward MT, Stoodley P. High velocity microspray enhance antimicrobial activity in *streptococcus mutans* biofilms. *J Dent Res* 2016;95:1494-500.
21. Fabbri S, Johnston DA, Rmaile A, Gottenbos B, De Jager M, Aspiras M, Starke EM, Ward MT, Stoodley P. *Streptococcus mutans* biofilm transient viscoelastic fluid behavior during high-velocity microsprays. *J Mech Behav Biomed Mater* 2016;59:197-206.

Instructions for Authors
The Journal of Clinical Dentistry

Mission Statement—*The Journal* is dedicated to the rapid publication of research and reviews focused on preventive oral healthcare products and new dental materials. Both laboratory and clinical research are accepted, as well as case reports. All scientific studies are blinded and peer-reviewed by an expert panel of researchers at independent academic institutions. *The Journal* also publishes issues dedicated to a single product and its research and development. These publications are designed to educate the dental professional on the safety and efficacy of these products so an informed and confident product recommendation can be made to patients. *The Journal* accepts no advertising. ***All papers accepted for publication will be assessed a placement fee of US$800 per published page.***

Manuscript Submission—All manuscripts are to be previously unpublished, in whole or in part, to be acceptable for review and publication. *The Journal* will be assigned all rights to works accepted for publication. Manuscripts, figures, and tables should be prepared in either Word or WordPerfect, and emailed as an attachment to EditorJClinDent@gmail.com. All manuscripts should be double-spaced and composed of the following sections: Abstract (Objective, Methods, Results, Conclusions), Introduction (with background of prior research and problem statement), Materials and Methods (how the research was conducted specifically), Results (with data and findings only), Discussion (author description of meaning of the results, conclusions, and directions for future research in the area), and References (formats listed below). Additionally, *The Journal* requires disclosure of the source for funding of the study, if any, in an Acknowledgment to appear at the end of the paper. The corresponding author will be identified, with e-mail address, following the Acknowledgment.

Manuscript Format—The following format applies to manuscripts; those which do not follow the format will be returned for adjustments.

- Abstracts are brief and are used only as a summary of the research.
- Tables are numbered using Roman notation (*e.g.*, I, II, III, IV, etc.) with centered titles and initial caps.
- Figures are numbered using Arabic notations (*e.g.*, 1, 2, 3, etc.) with descriptions to be placed below the figure.
- All tables and figures are to be referred to within the text to aid the reader.
- All named products should be followed by either a ™ or ®, and should include the product's manufacturer and location of same by city and country within parentheses.
- Indexing is used at the completion of an annual volume. As such, three to ten key words should accompany each paper.
- Author affiliations are encouraged, along with credentials such as DDS, DMD, PhD, etc.

Citations—All previous work or factual statements require documentation from the published literature. Citations should be numbered as they appear within the text and listed by the same number within the Reference section of the paper. For the convenience of the reader, citations in the text may only be listed by reference number, or if reference to the authors is made, only the first author should be listed followed by *et al*.When a citation has just two authors, both names should be cited in the text. All authors of a cited publication MUST BE LISTED within the Reference section of the paper (*et al*. is not accepted in Reference section). The following sample format applies to all references:

Book Source

Whole Book

Smith DF, Jones GH. *Dental Hygiene and Dental Practice*. 3rd Ed. Scientific Publisher, Philadelphia, 2010.

Chapter within Book

Black JK. Root scaling. In: *Dental Hygiene and Dental Practice,* Smith DF, Jones GH, eds. Scientific Publisher, Philadelphia, pp. 325-50, 2010.

Journal Source *(Please note new format)*

White DJ, Duschner H, Pioch T. Effect of bleaching treatments on microleakage of Class I restorations. *J Clin Dent* 2008;19:33-6.

Spelling and syntax used within the manuscript will be corrected using the Random House Dictionary of the English Language (American Version). All numbers in the text of ten or less should be written out (*e.g.*, one, five, ten). All numbers over ten should be given in numeric form (*e.g.*, 11, 15, 116). No abbreviations such as "vs." or "exam" should be used in place of "versus" or "examination."

Following manuscript review, the Senior Editor will compile the comments of the reviewers, along with his own, and correspond with the lead author detailing adjustments which will be required before a paper is considered "accepted." Re-submitted papers are thoroughly reviewed to confirm compliance with the comments.

Following acceptance, page proofs will be forwarded to the lead author for approval and assignment (sign-off). These must be returned as soon as possible to the Publisher with notations or corrections. All papers accepted for publication will be in print within 16 weeks of acceptance.

Contact Information	E-mail	Phone	Fax
Robert C. Emling, Editor	EditorJClinDent@gmail.com	+410-708-4980	+775-373-1989
Stephen M. Siegel, Publisher	Dntlpblshr@JClinDent.Com	+215-962-6251	+866-498-1977

The Journal of Clinical Dentistry
is printed on
recycled paper