NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS

SCHOOL OF HEALTH SCIENCES

DEPARTMENT OF DENTISTRY

POST-GRADUATE PROGRAM

SPECIALIZATION IN ORTHODONTICS

A RANDOMIZED, 3-MONTH, PARALLEL GROUP CLINICAL TRIAL TO COMPARE THE EFFICACY OF ELECTRIC 3D TOOTHBRUSHES VERSUS MANUAL TOOTHBRUSHES IN MAINTAINING ORAL HEALTH IN PATIENTS WITH FIXED ORTHODONTIC APPLIANCES

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ΕΘΝΙΚΟΝ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟΝ ΠΑΝΕΠΙΣΤΗΜΙΟΝ ΑΘΗΝΩΝ

ΤΜΗΜΑ ΟΔΟΝΤΙΑΤΡΙΚΗΣ

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Επιβλέπων Καθηγητής για την εκπόνηση της Μεταπτυχιακής Διπλωματικής Εργασίας κ. Χαλαζωνίτης Δημήτριος

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1. Χαλαζωνίτης Δημήτριος
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3. Πεπελάση Ευδοξία

Ευχαριστίες

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Περιεχόμενα

Περίληψη

Εισαγωγή: Οι ασθενείς που υποβάλλονται σε ορθοδοντική θεραπεία με ακίνητους ορθοδοντικούς μηχανισμούς εμφανίζουν συχνά αναποτελεσματικό έλεγχο της οδοντικής μικροβιακής πλάκας επειδή τα ορθοδοντικά αγκύλια, οι δακτύλιοι, τα ορθοδοντικά σύρματα και οι προσδέσεις προστατεύουν την οδοντική πλάκα από τη μηχανική δράση του βουρτσίσματος και της μάσησης. Οι ασθενείς αυτοί χρειάζονται επομένως υψηλό επίπεδο στοματικής υγιεινής για τη διατήρηση της οδοντικής τους υγείας. Η μηχανική απομάκρυνση της οδοντικής πλάκας αποτελεί τον σημαντικότερο παράγοντα της διατήρησης της στοματικής υγείας των ορθοδοντικών ασθενών.

Σκοπός: Στόχος της παρούσας μονά-τυφλής παράλληλου σχεδιασμού κλινικής δοκιμής ήταν η σύγκριση της αποτελεσματικότητας των ηλεκτρικών τρισδιάστατων οδοντοβουρτσών έναντι χειροκίνητων οδοντόβουρτσων στην αφαίρεσης της οδοντικής πλάκας και τη μείωση της φλεγμονής των ούλων.

Υλικά και μέθοδος: Το δείγμα αποτελείτο από 80 ασθενείς (40 αγόρια, 40 κορίτσια) με ακίνητους ορθοδοντικούς μηχανισμούς, οι οποίοι δεν χρησιμοποιούσαν ήδη ηλεκτρική οδοντόβουρτσα και δεν ήταν μέρος άλλης κλινικής δοκιμής.Τα κριτήρια επιλογής περιελάμβαναν ασθενείς μεταξύ 12 και 16 ετών με καλή γενική υγεία, ορθοδοντική θεραπεία χωρίς εξαγωγές ή αγενεσίες δοντιών, ουλίτιδα προκαλούμενη από μικροβιακή πλάκα, ενώ εξαιρέθηκαν ασθενείς με ενεργές τερηδόνες ή περιοδοντίτιδα, σύνδρομα και κρανιοπροσωπικές ανωμαλίες, αναπηρίες, περισσότερες από δύο αυχενικές και/ή όμορες εμφράξεις, προσθετικές εργασίες ή οδοντικά εμφυτεύματα, κάπνισμα, χρήση αντιβιοτικών ή άλλων φαρμάκων που οδηγούν σε υπερπλασία των ούλων. Οι ασθενείς τυχαιοποιήθηκαν σε δύο ομάδες και χρησιμοποίησαν είτε μια ηλεκτρική 3D ορθοδοντική οδοντόβουρτσα (Oral-B Pro-1000 με Oral-B Ortho head) είτε μια χειροκίνητη οδοντόβουρτσα (Oral-B Orthodontic brush). Στους ασθενείς δόθηκαν οδηγίες να βουρτσίζουν δύο φορές την ημέρα για δύο λεπτά. Τα κύρια αποτελέσματα ήταν η απομάκρυνση της οδοντικής πλάκας με τη χρήση του τροποποιημένου δείκτη πλάκας Silness και Löe (PI-M) και του τροποποιημένου δείκτη στοματικής πλάκας (FMPS-M) και η μείωση της φλεγμονής των ούλων με τον τροποποιημένο

ουλικό δείκτη Gingival (GI-M) 1963) και τροποποιημένο απλουστευμένο ουλικό δείκτη (GI-SM). Οι μετρήσεις έγιναν στην αρχή, έναν, δύο και τρεις μήνες μετά. Η τυχαιοποίηση πραγματοποιήθηκε με δύο τυχαίες ακολουθίες, μία για κάθε βούρτσα και οι τιμές ακολουθίας ήταν γραμμένες και σφραγισμένες σε αδιαφανείς αριθμημένους φακέλους. «Τυφλός» κατά την διάρκεια της δοκιμής ήταν μόνο ο ερευνητής που μετρούσε τους δείκτες.

Στατιστική ανάλυση:Περιγραφικά στατιστικά στοιχεία υπολογίστηκαν για όλες τις μεταβλητές. Γραμμικά μεικτά μοντέλα υπολογίστηκαν για κάθε μία από τις 4 κύριες μεταβλητές με τυχαίους συντελεστές σημείου τομής και κλίσης, τον χρόνο ως συν-μεταβλητή και μη δομημένο τύπο συνδιακύμανσης. Τα μοντέλα συγκρίθηκαν μεταξύ τους με τα κριτήρια Akaike'sInformationCriterion (AIC) και Schwarz'sBayesianInformationCriterion (BIC). Η ανάλυση έγινε με το λογισμικό IBM SPSS Statistics for Windows, έκδοση 25.0.

Αποτελέσματα: Παρατηρήθηκε σημαντική ποικιλότητα μεταξύ των ασθενών ως προς τις τιμές όλων των εξαρτημένων μεταβλητών. Ο παράγοντας ‘βούρτσα’ δεν παρέμεινε ως στατιστικώς σημαντικός παράγοντας σε κανένα μοντέλο για καμία από τις 4 κύριες εξαρτημένες μεταβλητές. Ο παράγοντας ηλικία είχε αρνητική συσχέτιση με τους δείκτες GI, FMPS-M και GI-SM, οι οποίοι έδειχναν πτωτική τάση όσο μεγαλύτερη ήταν η ηλικία, χωρίς όμως να αποτελεί κυρίαρχο παράγοντα.

Συζήτηση: Έναν από τους περιορισμούς της κλινικής αυτής δοκιμής αποτελεί η μειωμένη διακριτική ικανότητα των δεικτών FMPS και GIS οι οποίοι λαμβάνουν εκατοστιαίες τιμές με αποτέλεσμα την ύπαρξη πολλών ακραίων τιμών. Οι τιμές (κατάλοιπα) των δεικτών δεν ακολουθούσαν κανονική κατανομή με αποτέλεσμα την αμφισβήτηση της εγκυρότητας τους. Περιγραφικά στατιστικά χρησιμοποιήθηκαν κατά τα οποία δεν προέκυψε στατιστικά σημαντική διαφορά για τους δείκτες αυτούς. Αξίζει επίσης να σημειωθεί η διεύρυνση του αρχικού ηλικιακού εύρους των ασθενών κατά ένα χρόνο λόγω δυσκολίας συμπλήρωσης τους δείγματος και με σκοπό να ολοκληρωθεί εγκαίρως η μελέτη. Στα πλεονεκτήματα της κλινικής αυτής δοκιμής συγκαταλέγονται το διάστημα παρακολούθησης των ασθενών το οποίο είναι επαρκές σύμφωνα με τις προδιαγραφές της ADAαλλά και μεγαλύτερο από κάθε άλλη αντίστοιχη μελέτη παράλληλου σχεδιασμού στην βιβλιογραφία. Τα χρονικά ωστόσο διαστήματα παρακολούθησης των ασθενών δεν ήταν όμοια για αυτό ελήφθη υπόψη ο

πραγματικός χρόνος παρακολούθησης των ασθενών στο γραμμικό μεικτό μοντέλο ανάλυσης. Πλεονέκτημα αποτελεί ακόμα ο παράλληλος σχεδιασμός της μελέτης ο οποίος χρειαζόταν μεγαλύτερο δείγμα αλλά είναι μεγάλης ερευνητικής αξίας. Τέλος πλεονέκτημα αποτελεί η τυχαιοποίηση του δείγματος αλλά και η διεξαγωγή της ως «μονά-τυφλή» («τυφλός ο ερευνητής που πραγματοποιούσε τις μετρήσεις).

Συμπεράσματα:Από τηνμελέτη αυτή δεν προέκυψε καμία διαφορά στην αποτελεσματικότητα της ηλεκτρικής 3Dέναντι της χειροκίνητης οδοντόβουρτσας στην απομάκρυνση της μικροβιακής πλάκας και την βελτίωση της ουλίτιδας σε ασθενείς με ακίνητους ορθοδοντικούς μηχανισμούς. Επομένως, οι ορθοδοντικοί θα πρέπει να επικεντρωθούν στην βελτίωση της στοματικής υγιεινής των ασθενών τους με την συνεχή χορήγηση οδηγιών, συνεχείς ελέγχους της τερηδόνας και της υγείας των ούλων και χορήγηση συμπληρωματικών μέσων ανεξαρτήτου της βούρτσας που χρησιμοποιείται.

Abstract

Introduction: The objective of this single-blinded, parallel group clinical trial was to determine plaque removal efficacy and gingival inflammation reduction comparing electric 3D toothbrushes versus manual toothbrushes in orthodontic patients.

Methods: Eighty adolescents with fixed orthodontic appliances in both arches no currently using electric toothbrushes or participating in other trials were randomized in 1:1 ratio with equal number of both sexes, in this parallel examiner blinded clinical trial. Eligibility criteria included ages between 12 and 16 years with good general health, non-extraction orthodontic treatment or tooth agenesis, plaque-induced gingivitis excluding patients with active caries or periodontitis, syndromes and craniofacial deformities, disabilities , more than two cervical and/or proximal fillings, dental prostheses or dental implants, smoking, using antibiotics or other medication resulting in gingival enlargement. Patients were assigned to use either an electric 3D orthodontic toothbrush fitted (Oral-B Pro-1000 with Oral-B Ortho head) or a manual toothbrush (Oral-B Orthodontic brush) and instructed to brush twice a day for two minutes. The main outcomes were plaque removal assessed with the use Modified Silness and Löe plaque index (PI-M) and Modified Full mouth plaque score (FMPS-M) and gingival inflammation reduction assessed with Modified Gingival index (GI-M) (Löe & Silness 1963) and Modified Simplified Gingival index (GI-SM). Measurements were made at baseline, one, two and three months.Stratified randomization was accomplished with two random sequences, one for each brush and sequence values written and sealed in opaque numbered envelopes. Blinding was applicable for outcomeassessment only.

Results: Considerable variability was observed among patients in the values of all dependent variables. The 'brush' factor did not remain a statistically significant factor in any model for any of the four major dependent variables. The factor age had a negative correlation with the GI, FMPS and GIS indicators, which showed a decreasing trend as patients getting older, but it was not a dominant factor

Conclusions: No difference was found in efficacy amongelectric 3D and manual and toothbrush in adolescents with fixed orthodontic appliances concerningplaque removal efficacy and

gingival inflammation reduction. Therefore, orthodontists should focus onenhancing their patients' dental awareness and oralhygiene along with professional prophylaxis and other oral hygiene aids independently the brush used.

Introduction

Protocol and funding

The protocol of this randomized clinical trial was based in the recommendations of the SPIRIT 2013 Statement and registered in ClinicalTrials.gov with identifier number NCT02699931. Ethics Committee (EC) of the School of Dentistry, UoA the EC approved the protocol on March 15, 2016(protocol number: 290); such approval is mandatory for commencement of any clinical research at the School. Concerning funding, electric and manual toothbrushes and toothpastes for all participants were provided by Procter & Gamble (Oral-B). Procter & Gamble had no role in the design of this study and did not have any role during its execution, analyses, interpretation of the data, or decision to submit results. Miscellaneous costs were covered by the participating departments. No other funding deemed necessary.

Literature Review

Patients undergoing orthodontic treatment with fixed appliances need a high level of oral hygiene to maintain dental health. Orthodontic patients often show ineffective plaque control because fixed appliances, such as brackets, bands, archwires and ligatures shield dental plaque from the mechanical action of brushing and mastication. Undisturbed supragingival plaque initiates gingival inflammation and hyperplasia and may cause caries and enamel white spots. Despite the use of mouthwashes and topical fluorides, mechanical removal of plaque remains the most important factor of oral hygiene during orthodontic treatment. Flossing often becomes more difficult and time demanding when fixed orthodontic brackets are present. As a result, effective toothbrushing plays the most important role as a preventive measure in these patients.

Unfortunately, the majority of patients do not invest enough time to brush their teeth properly and the situation becomes even worse with orthodontic appliances. Inadequate brushing leads to plaque increase and subsequently to gingival inflammation and bleeding, gingival enlargement, and increased pocket depths. Furthermore, microbial changes in the subgingival periodontal flora are associated with placement of orthodontic brackets: gram positive cocci

decrease and spirochetes, motile rods and other gram negative organisms such as Actinobacillus, Bacteroides, and Prevotella increase (Atak et al., 1996).

Randomized clinical trials have assessed the efficacy of various types of toothbrushes regarding two main areas of interest: plaque removal and gingival inflammation. Many studies conclude that electric toothbrushes offer statistically significant benefits versus manual brushes in at least one of these areas (Ho HP et al., 1997; Clerehugh et al., 1998; Borutta et al., 2002; Costa et al., 2007; Klukowska et al., 2013; Erbe et al. 2019), but other studies found no statistical difference between the two types of brushes (Heasman et al., 1998; Thienpont et al., 2001; Hickman et al., 2002; Costa et al., 2010). Some conclude that manual brushes are better in at least one area (Trimpeneers et al., 2001). In general, electric toothbrushes performed at an equal level with manual toothbrushes with regard to plaque index and gingival index but they were found to perform more superiorly in reducing the incidence of bleeding on probing and interdental bleeding.

Recent systematic reviews and meta-analyses investigated whether manual or electric toothbrushes were more effective in achieving good oral health in the orthodontic patient. Kaklamanos et al. (2008) and Huang (2009) concluded that current evidence was insufficient to support the comparative efficacy of electric toothbrushes in reducing gingivitis in patients undergoing fixed orthodontic appliance therapy. D'Costa et al. (2011) concluded that although it is likely that electric toothbrushes provide some improvements in oral health compared to manual toothbrushes, these improvements are not strong enough to justify electric toothbrushes' greater cost. Makhmari et al. (2017) concluded that powered toothbrushes may promote gingival health better than manual toothbrushes in orthodontic patients but no type demonstrated clear superiority and future studies are necessary to elucidate the clinical relevance of these results.

Need for a trial

Electric toothbrushes are continually being improved by the manufacturers and some of the improvements might have a substantial clinical effect. Studies investigating the efficacy of the latest '3D' toothbrushes - which exhibit two actions (rotation / oscillation and pulsation) - on plaque removal and gingival health on an orthodontic population were not able to prove 3D

electric toothbrushes' superiority with sufficient evidence (Thienpont et al., 2001; Hickman et al., 2002; Costa et al., 2007; Costa et al., 2010; Klukowska et al., 2013).

A randomized clinical trial was therefore needed in order to evaluate whether 3D electric orthodontic toothbrushes are more effective in reducing plaque and gingival inflammation in orthodontic patients, compared to manual orthodontic brushes. We expect this trial's results to assist clinicians and orthodontic patients in selecting the brush most effective at preventing gingival inflammation, caries and white spots.

Specific hypothesis

Our research hypothesis was that the 3D electric toothbrush is superior to the manual toothbrush in removing plaque and reducing the occurrence and severity of gingivitis in patients with fixed orthodontic appliances.

Materials and Methods

Trial design

This trial was designed as a randomized, controlled, investigator blinded superiority trial, with two parallel groups and a 1:1 allocation ratio. Equal number of males and females was allocated to each group.

Participants and settings

The trial was conducted at the Department of Orthodontics of the National and Kapodistrian University of Athens, School of Dentistry. The trial was held in Greece at what is an urban location (Athens). Patients were treated by residents of the DoO, supervised by the faculty. This is an academic environment setting and results may not be generalizable to private offices.The duration of the study was 3 months. We followed the recommendations of Robinson et al. (2006), Kaklamanos et al. (2008) and D'Costa et al. (2011) who question the validity of studies shorter than two months, due to their potential inability to account for novelty effects.

Eligibility Criteria

Inclusion Criteria

Patients eligible for the trial should comply with all of the following at randomization:

Age between 12 and 16 years

This age group represents the majority of patients seeking orthodontic treatment and is homogeneous regarding occupational status (high-school and lyceum students in Greece). Younger patients might present with cooperation problems, whereas older patients might be less homogeneous regarding social status and other factors.

Good general health

Based on a recent medical history.

Fixed orthodontic appliances

Patients should have fixed labial appliances (brackets) on all teeth from central incisor to first molar, in both the maxillary and the mandibular arch. Fixed appliances should have been placed at least two months before the patient is accepted into the study and no more than two years.

Patients were not accepted if remaining treatment was estimated at fewer than 3 months. All brackets should be metallic (conventional, not self-ligating). There were no restrictions regarding brackets' manufacturer and size. Molars should be banded and all other teeth bonded.

Non-extraction orthodontic treatment

The outcomes were evaluated at all teeth from first molar to first molar.

Plaque-induced gingivitis.

Patients were included if they had gingival bleeding on at least 30% of the sites examined using the criteria for bleeding of the Modified Simplified Gingival Index (as described in section 12). A minimum level of gingival bleeding is needed in order to be able to demonstrate some improvement in gingival health with effective toothbrushing.

Exclusion Criteria

Patients were excluded for any of the following reasons:

Active caries

Periodontitis

Tooth agenesis (excluding third molars)

Syndromes and craniofacial deformities

Current use of electric toothbrush

More than two cervical and/or proximal fillings

Dental prosthesis or dental implants

Smoking or use of other tobacco products

Antibiotics during the last 2 months

Medication that may result in gingival enlargement (anticonvulsants, immunosuppressants, and calcium channel blockers

Disabilities that might affect toothbrushing skills(manual dexterity, mental disabilities)

Peri-oral or intra-oral piercing

Cardiac or other medical condition that requires antibiotic prophylaxis for dental treatment

Participation in other trials

Consent / assent

Parents/guardians provided written informed consent and patients provided written assent before randomization and before any procedures applied. Consent and assent forms are included in Appendix 1 and 2.

Interventions

Eligible patients were randomly allocated at a 1:1 ratio between Group A - electric toothbrush and Group B - manual toothbrush. The brushes were delivered by the same investigator (DJH) to both groups. Participants were asked to brush twice daily, once after lunch and once before night sleep. Patients were taught how to brush at the commencement of the study. Primary outcomes were assessed at monthly intervals. The investigator assessing was blinded to the brush used.

Brushing instructions were given verbally to all patients and the time spent for instructions was ten minutes for each patient. Patients were instructed to brush for two minutes (Van der Weijden et al., 1993, Ay et al., 2007, Van der Weijden et al., 2008). Instructions given verbally to the patients are described below.Timers (2 minutes) were provided to Group B patients.

The brushing technique for electric brushes was as recommended by the manufacturer, i.e.:

• Wet brush head and apply toothpaste. To avoid splashing, guide the brush head to your teeth before switching on the appliance. Guide the brush head slowly from tooth to tooth, spending a few seconds on each tooth surface (Figure 1). Start brushing the outsides, then the insides and finally the chewing surfaces. Brush all four quadrants of your mouth equally. Do not press too hard, simply let the brush do all the work.

• Helping protect your teeth and gums from hard brushing, your toothbrush has a pressure control feature installed. If too much pressure is applied, the red pressure sensor light will light up, reminding you to reduce pressure. In addition the movement of the brush head will

continue but its pulsation will stop and you will also hear a different sound while brushing. Periodically check the operation of the pressure sensor by pressing lightly on the brush head during use.

• A short stuttering sound at 30-second intervals reminds you to brush equally all four quadrants of your mouth. A long stuttering sound indicates the end of the professionally recommended 2-minute brushing time.

The brushing technique for manual brushes was the following:

• Brush the outside tooth surfaces (labial and buccal): Hold your brush in the palm so that the bristles of the head are between the brackets and the gums and angled towards the brackets (at an angle of approximately 45°) and take care that the bristles contact your gums, teeth and brackets. Use short back-and-forth strokes.

• Reposition the brush so that the bristles contact the part of the tooth that is occlusa to the bracket and angle the bristles towards the bracket. Repeat the stroke movement. Make sure that the bristles invade between the tooth and the wire.

• Continue from the back to the front of the mouth. Do not brush more than two teeth simultaneously.

• Brush the occlusal surfaces of the back teeth: Hold the brush so that the bristles point towards the occlusal surfaces and stroke back and forth.

• Brush the inside surfaces (lingual and palatal): Hold the brush so that the bristles point towards the gums at an angle of 45°. Use short back-and-forth strokes, then roll the brush towards the occlusal surfaces.

• Always hold the brush head horizontal when cleaning the outside surfaces of the teeth. It is easier to hold the head vertically when brushing the inside surfaces of the top and bottom teeth.

• Avoid too much pressure and fast movements and remember to contact the gum line. Also avoid brushing too vigorously to prevent damage to the gums. When cleaning the teeth keep using the same sequence of brushing.

• Use the timer given so that you brush for about two minutes.

• Remember to thoroughly clean the brush when finished.

Orthodontic treatment

No restrictions were imposed on orthodontic treatment, including archwires (type, size and material). In case the archwire had loops and bends that potentially shielded dental plaque, this was noted. All brackets were metallic (conventional, not self-ligating).

Although it is generally believed that elastic ligatures retain more plaque, no difference in GI has been observed between elastic and steel ligatures (Türkkahraman et al., 2005), or between conventional brackets with elastic ligatures and self-ligated brackets (Buck et al., 2011; Cardoso et al., 2015), so there was no restriction concerning type of ligatures (wire or elastic) in this study. The treating clinicians were asked to refrain from commenting on the oral hygiene of the patient, from providing oral hygiene instructions and from performing tooth cleaning. Such instructions and procedures were provided by the investigators, as described in other sections. The toothbrushes, both electric and manual, do not cause harm, disturbances or allergic reactions to patients so not any modifications were needed.

During the study

• Patients were asked not to use other toothbrushes and toothpastes except the ones given to them as part of the study.

• Patients were asked not to floss or use interdental brushes.

• Patients were asked not to use whitening or fluoride products.

• Patients were asked to inform us if they visit their dentist for treatment, including cleaning, periodontal treatment or topical fluoridation.

• Patients were asked not to take part in other trials.

Outcomes

The primary outcomes were plaque accumulation and gingival inflammation. Only labial surfaces of all bonded teeth were measured and scored for all primary outcome measures. Banded molars were measured and scored only for GI-M and GI-SM indices.

Modified Silness and Löe plaque index (PI-M)

The Silness and Löe index (Silness and Löe, 1964) does not take into account the pattern of plaque accumulation in orthodontic patients. To overcome this problem, Williams et al. (1991) divided the tooth into mesial, distal, gingival, and incisal regions in relation to the bracket and scored plaque in each region using the four codes of the original index (0 to 3) (Table 1). The values are summed to obtain a total score, which ranges from 0 to 12 for each tooth. This modified index is recommended for patients with fixed orthodontic appliances because it acknowledges the usual effects of orthodontic appliances on plaque distribution and has much greater categorical discrimination (Clerehugh et al., 1998; Thienpont et al., 2001; Costa et al., 2007; Al-Anezi et al., 2012).

However, it is not always possible to evaluate plaque in the gingival region, due to soft tissue inflammation and gingival enlargement, which are common during orthodontic treatment. Moreover, brackets are often placed adjacent to the crest of the gingiva on teeth that are only partially erupted, such as second premolars and second molars. For the purpose of this study, no plaque scores were measured at the gingival region of such teeth where brackets are closely neighboured by soft tissues. Thus, the maximum score for a tooth of this category was 9 instead of 12 (number of evaluated surfaces × 3).

The total score of each tooth was divided by its individual maximum score in order to obtain a tooth average. The patient average was computed as the average across all evaluated teeth. Only labial surfaces of all bonded teeth were measured. For the PI-M, four areas of the labial aspect of each bonded tooth were scored, as described above. Banded molars were not measured.

Modified Full mouth plaque score (FMPS-M)

The Plaque Control Record or full mouth plaque score (FMPS) as described by O'Leary et al. (1972) records the presence and absence of plaque on individual tooth regions (mesial, buccal, distal, lingual). While scoring, no attempt is made to differentiate between varying amounts of plaque on the tooth surfaces. All teeth and all tooth regions (mesial, buccal, distal, lingual) are

examined and scored. The FMPS index is derived by dividing the number of plaque containing regions by the total number of available tooth regions. It is expressed as a percentile.

In the present study a modification of the FMPS (FMPS-M) was used, since only the labial surfaces of the bonded teeth were be measured and scored. Three regions of the labial surface of each bonded tooth were scored (mesial, buccal, distal). The FMPS-M index (in percentile) was derived by dividing the number of plaque containing labial surfaces by the total number of available labial tooth surfaces. Banded molars were not measured.

Modified Gingival index (GI-M)

The Gingival Index (GI) is a measure of the severity of gingivitis and is scored by measuring the amount of gingival inflammation, also considering redness and bleeding (Löe & Silness 1963). The Gingival Index (GI) first described by Löe & Silness (1963) was later slightly modified by Löe (1967) (Modified Gingival Index) in terms of the way the periodontal probe was used while examining (Table 2). Nowadays, Löe's modification is used. This gingival index is the most widely used, so our resultsare comparable to most other studies. The index is computed as the average of the measurements of the individual GI on all tooth regions (mesial, buccal, distal, lingual) of all teeth according to the following scale:

In the present study a modification of the GI (GI-M) was used, where only the labial surfaces of the bonded teeth were measured and scored. Three regions of the labial surface of each bonded tooth were scored (mesial, buccal, distal), as described above. Banded molars were also measured.

Modified Simplified Gingival index (GI-SM)

The simplified gingival index (GI-S) as described by Lindhe et al. (1982) records the presence of bleeding upon probing the gingival crest. While scoring, no attempt is made to differentiate between varying severity of bleeding. All teeth and all tooth regions (mesial, buccal, distal, lingual) are examined and scored. The GI-S score is derived by dividing the number of bleeding regions by the total number of available tooth regions. It is expressed as a percentile.

In the present study, a modification of the GI-S (GI-SM) was used, since only the labial surfaces of the bonded teeth were measured and scored. Three regions of the labial surface of each

bonded tooth were scored (mesial, buccal, distal). The FMPS-M index (in percentile) was derived by dividing the number of bleeding labial surfaces by the total number of available labial tooth surfaces. Banded molars were also measured.

Participant Timeline

Initial visit(s)

Procedures took place in the following order:

- Screened by a faculty member
- Initial screening considered the following criteria: age, treatment plan: non-extraction, fixed orthodontic appliances, no tooth agenesis, no syndromes or craniofacial deformities.
- Evaluated by investigator
  If fulfilling all criteria then:
- Informed about the study
- Obtain the consent/assent form
- Enrolled in study
- Baseline measurements (time point T0)
- Sent for randomization
- Randomized to group A or B
- Brush provided, brushing instructions

Patient monthly visits

Visits were planned at intervals of 4 weeks, in line with the scheduled orthodontic visits. A margin of ±1 week was allowed.

- Visit 1 (4 weeks) time point T1
- Visit 2 (8 weeks) time point T2
- Visit 3 (12 weeks) time point T3
- Final interview at T3 (12 weeks)

Interview with the participant, give brushes to patient as a gift, instructions for electric toothbrush, if not already given. (Table 3)

Sample Size

The sample size was calculated on the basis of the primary hypothesis. Analyzing two of the studies we found the following:

Klukowska et al. (2011) reported the following values for plaque at the gingival region average: 57.33, SD: 28.17, range: 3 to 100 (these are percentage of tooth covered by plaque, as assessed by the digital method). Using these values, and assuming the customary 5% and 80% alpha and power levels, the following table gives the required sample size for a parallel design study, when the difference to be detected ranges from 10% to 40% (Table 4)

Clerehugh et al. (1998) reported values for the orthodontic modification of the plaque index. SD was around 0.3 and the average values ranged from 1 to 1.5 approximately. The following table shows calculated sample sizes for detecting a difference in means, expressed as a percentage, ranging from 10% to 40% (we assume a population mean of 1.25 and an SD of 0.30) (Table 5).

The above tables show comparable results. A detection of 20% difference is feasible with a sample size of 35-40 subjects in each group, to cover potential drop-outs. The ADA Council on Scientific Affairs (2012) recommends aiming for detection of a 15% difference and including at least 25 subjects. We decided on a sample size of 40 participants per group.

Randomization

Stratified randomization was used and patients were allocated at a 1:1 ratio between Group A - Electric toothbrush and Group B - Manual toothbrush, for each sex separately. Investigator not brush-blinded obtained two random sequences from www.random.org (List Randomizer service), one for the male group and one for the female group. Each sequence was a random ordering of a list of 20 ‘E’s and 20 ‘M’s (E: Electric, M: Manual) and the sequence values were written on standard-sized pieces of paper using a pencil and sealed in opaque numbered envelopes (sequentially numbered from F1 to F40 (female group) and M1 to M40 (male group)) by a person not involved in the project. All patients who give consent for participation and fulfill the inclusion criteria were allocated by the investigator for initial interviews, recruitment and clinical measurements. Allocation envelopes were kept away from the investigators locked accessible only to a secretarial staff member not involved in the project. On new patient recruitment, the next numbered envelope from the male or female pack was retrieved and the name of the patient was written on the envelope.

Blinding

Clinical measurements of plaque accumulation and gingival inflammation were conducted by an assessor blinded to treatment allocation. Due to the nature of the intervention, neither participants nor investigator offering the brushes can be blinded to allocation.

Statistical analysis

Descriptive statistics were computed for all variables. Linear mixed effects models were fitted to each of the dependent variables of the primary outcomes (PIM, FMPS, GI, GIS) using a random coefficients model (intercept and slope), time from baseline as a covariate and an unstructured covariance type. All main effects (time, age, sex, brush) and all 2-way interactions were entered into a full model and each factor was sequentially removed if $p > 0.05$. We used the maximum likelihood estimation method (ML) and compared nested models by Akaike's Information Criterion (AIC) and Schwarz's Bayesian Information Criterion (BIC). Bootstrapping (10,000 samples) was applied to the final model to compute estimates of the fixed effects and covariance parameters. The residuals were evaluated by visual inspection of Q-Q plots. IBM SPSS Statistics for Windows version 25.0 (IBM Corp., Armonk, NY, USA) was used for the analysis. Graphs were prepared with Microsoft Excel (Microsoft Corp., USA).

Interim analyses and stopping guidelines

Not applicable.

Harms

No serious harm was observed other than gingivitis associated with plaque accumulation.

Results

Descriptive statistics of the variables are presented in Table 6.

Plaque index modified (PIM)

The time profile plots for each individual of the Electric and Manual groups showed large interindividual differences in both intercept and slope. This was reflected in the intraclass correlation coefficient (ICC) computed from the estimates of the covariance parameters of the unconditional mean model (Model PIM-1); 56% of the variation was attributed to between-patients differences (for all model details see Supplementary Text).

The second model (Model PIM-2) tested for variations over time by including time as a fixed and random factor. There was a significant decrease of PIM over time (beta = -0.0067, SE = 0.0030, p = 0.031). A significant difference in intercept and slopes between patients was also found, indicating that part of the variance could be explained by interindividual predictors.

We hypothesized that there might be a transient improvement in oral hygiene due to the novelty in participating in a research project or in using an electric toothbrush (Hawthorne effect), so we modelled the response over time as a cubic growth curve: we expected an initial decrease in PIM followed by a gradual return to the initial values and levelling thereof. We compared this to a quadratic model and to the previous linear model but no significant findings emerged and these models were abandoned (results not shown).

The model of interest (Model PIM-3) was constructed by adding brush and its interaction with time to the previous model. These factors were not found to be significant (p = 0.971 and p = 0.891 for brush and time * brush, respectively).

The full model (Model PIM-4) was constructed by including age (centered on the average value of 14 years), sex and brush, and all 2-way interactions, as fixed factors. Only the interaction of sex * time was found significant (p = 0.015) and this was retained; all other interactions were removed and the model was recomputed (Model PIM-5). Based on the p values, the factors age and brush were subsequently also removed (p = 0.091 and p = 0.727 for age and brush, respectively). The final model included sex, time and their interaction (Model PIM-6).

The criteria computed by SPSS for model comparison were inconsistent. Although AIC and AICC indicated that PIM-6 might be better than PIM-2, CAIC and BIC showed the opposite. However, the difference between the AIC values was only 1.57 which makes both models plausible, whereas the difference in BIC values was larger. In any case, it is clear that brush was not a significant factor in any model considered.

The Q-Q plot of the residuals of Model PIM-6 showed a few potential outliers. We tested the robustness of the model by removing the largest outliers (n=5 out of 320: 1.6%) and recomputing the model (Model PIM-7). The interaction term and the sex factor were not significant anymore and were removed, resulting in a model identical to Model PIM-2 (Model PIM-8: only time included as a fixed and random factor).

Gingival index modified (GI)

The time profile plots for each individual of the Electric and Manual groups showed large interindividual differences in intercept but no clear slope differences. The intercept variation was reflected in the intraclass correlation coefficient (ICC) computed from the estimates of the covariance parameters of the unconditional mean model (Model GI-1); 67% of the variation was attributed to between-patients differences.

The second model (Model GI-2) tested for variations over time by including time as a fixed and random factor. There was no significant change of GI over time (beta = -0.0018, SE = 0.0034, p = 0.590) and no significant interindividual differences in slope.

The full model (Model GI-3) was constructed by including age (centred on the average value of 14 years), sex and brush, and all 2-way interactions, as fixed factors to the initial model (GI-1). No interactions were found significant and these were removed to compute a model with main effects only (GI-4). Age was the only significant predictor found (b = -0.017698, SE = 0.007750, p = 0.025). The final model was computed after removing all other factors except for age (GI-5).

Model comparison showed that there was a statistically significant effect of age on GI, but the difference compared to the unconditional model was marginal.

The Q-Q plot of the residuals of Model GI-5 did not show any evidence of non-normality.

Full mouth plaque score index modified (FMPS)

The time profile plots for each individual of the Electric and Manual groups showed large interindividual differences in intercept. The intercept variation was reflected in the intraclass correlation coefficient (ICC) computed from the estimates of the covariance parameters of the unconditional mean model (Model FMPS-1); 65% of the variation was attributed to between-patients differences.

The second model (Model FMPS-2) tested for variations over time by including time as a fixed and random factor. There was no significant change of FMPS over time (beta = -0.002795, SE = 0.003507, p = 0.428) but evidence of interindividual differences in slope (p = 0.033).

The full model (Model FMPS-3) was constructed by including age (centred on the average value of 14 years), sex and brush, and all 2-way interactions, as fixed factors to the linear time model (FMPS-1). No interactions were found significant and these were removed to compute a model with main effects only (FMPS-4). Age and sex were the only significant predictors (b = -0.025560, SE = 0.007576, p = 0.001 and b = 0.044381, SE = 0.022323, p = 0.050 for age and sex, respectively). We also computed models with age and sex, and age alone (FMPS-5, FMPS-6).

Model comparison showed that the last two models were comparable.

Simplified Gingival index modified (GIS)

The time profile plots for each individual of the Electric and Manual groups showed large interindividual differences in intercept. The intercept variation was reflected in the intraclass correlation coefficient (ICC) computed from the estimates of the covariance parameters of the unconditional mean model (Model GIS-1); 68% of the variation was attributed to between-patients differences.

The second model (Model GIS-2) tested for variations over time by including time as a fixed and random factor. There was no significant change of GIS over time (beta = -0.000543, SE = 0.004159, p = 0.897) and no evidence of interindividual differences in slope (p = 0.542).

The full model (Model GIS-3) was constructed by including age (centred on the average value of 14 years), sex and brush, and all 2-way interactions, as fixed factors to the initial model (GIS-1). No interactions were found significant and these were removed to compute a model with main

effects only (GIS-4). Age was the only significant predictor (b = -0.027035, SE = 0.009244, p = 0.004). The final model was computed after removing all other factors except for age (GIS-5).

Model comparison showed that there was a statistically significant effect of age on GIS, but the difference compared to the unconditional model was marginal.

Discussion

Adequate plaque control is important for patients undergoing fixed orthodontic treatment as bands, brackets, wires and ligatures trap food and debris which frequently leads to plaque accumulation. This aggravates gingivitis, hyperplastic tissue, dental caries, decalcification and white spot lesions. Various types of toothbrushes are available in the market so there is a need for clinical trials to evaluate their effectiveness in order to guide professional recommendations for orthodontic patients. Numerous clinical studies have been conducted in patients receiving fixed orthodontic treatment which compared the effectiveness of different types of manual and powered toothbrushes with conventional and advanced designs. However, the results were found to be conflicting(Kaklamanos et al. 2008 and Huang 2009D'Costa et al. 2011Makhmari et al. 2017). This randomized controlled study attempted to give important information on the efficacy of a 3D powered toothbrush with a dedicated orthodontic head, compared to a manual orthodontic toothbrush, on the oral health of orthodontic patients undergoing fixed appliance therapy in a university clinic.

The parallel group design, which was used in our study, is useful to incorporate stratification into the randomization process to ensure relative balance with respect to important prognostic factors at baseline, thus lessening the likelihood that the final study results will be confounded by baseline differences between the study groups. A crossover design, enabling each brush to be tested in each subject, is also employed in many comparative toothbrushing studies in orthodontic patients (Thienpont et al. 2001, Costa et al. 2007, Costa et al. 2010, Erbe et al. 2013,Klukowska et al 2013). Crossover studies are feasible when the condition studied is relatively stable, the intervention has a short term effect and adequate washout periods are easy to interpret. The risk of patients' attrition with the first intervention/brush also may increase because of prolonged study duration. For all these practical reasons we preferred the parallel design (one more study with parallel design found (Hickman et al. 2002). On the other hand, crossover RCTs can directly compare the interventions in regard to effectiveness, adverse effects and ease of use, and provide an overall choice so a future study with the same comparators and cross over design can be addressed.

Tooth brushing duration also varies between studies. To remove the potential bias that this variable would introduce in our trial, subjects allocated to the manual toothbrush were issued a hourglass timer and instructed to brush twice daily for a timed two minutes. This procedure has been used in other studies (Clerehugh et al. 1998, Heasman et al. 1998, Trimpeneers et al. 2001). Subjects allocated to the powered toothbrush were given identical instructions andthe brush had an integral 30 second timer, therefore, tooth brushing duration was standardized between groups. Clerehugh et al. 1998 used a similar duration althoughother investigators have employed a two-minute toothbrushing time only for subjects allocated to the manual toothbrushand three minutes to the powered brush (Heasman et al. 1998).

Plaque indices used in non-orthodontic population do not account adequately for the particular plaque retention problems posed by fixed appliance components. A modification of the plaque index, developed specifically for subjects with fixed orthodontic appliances, was used in the present study. It has been employed in other trials comparing a powered and a manual toothbrush in fixed appliance orthodontic patients (Clerehugh et al., 1998; Thienpont et al., 2001; Costa et al., 2007; Al-Anezi et al., 2012). In the study reported here, plaque wasonly assessed on the buccal surfaces of teeth that werebonded but not banded (molars) due to difficulty in plaque assessment. The lingual surfaces, which other reportshave noted were improved considerably in non orthodonticsubjects by use of a powered brush (Warren et al. 1996), were not included inanalyses. Although this approach has been used in anothersimilar trial (Clerehugh et al., 1998) it is possible that it has increased the risk ofmaking a Type II error through exclusion of regions wherethe difference between the groups may be largest.

The duration of the study was designed to be 3 months. We followed the recommendations of ADA as well as those of Robinson et al. (2006), Kaklamanos et al. (2008), D'Costa et al. (2011) and Makhmari et al. (2017), who question the validity of studies shorter than two months, due to their potential inability to account for novelty effects. Our study assessed the interventions for a longer time span than similar parallel studies found in the literature. The time between each assessment was not the same for each patient, so time was entered intothe general mixed-effects linear modelsas a covariate.

The original protocol of the study was followed as planned except for the age limits of the inclusion criteria. Due to difficulties in recruitment, and in order to complete the study within the planned time period, we relaxed these limits by a year and thus included 7 subjects that were beyond the original limits. We do not expect that might affect the results, as the age extension, and the number of patients, was small.

When the toothbrush groups were compared, no statistically significant differences observed for any of the parameters assessed time points the study. This confirms the findings of studies (Clerehugh et al. 1998, Heasman et al. 1998), where other types of orthodontically dedicated powered toothbrushes have been compared to manual toothbrushes in fixed appliance patients. The 'brush' factor did not remain a statistically significant factor in any model for any of the four major dependent variables. The factor age had a negative correlation with the GI, FMPS and GIS indicators, which showed a decreasing trend as patients getting older, but it was not a dominant factor. The factor ‘sex’ showed a correlation with PIM, which was found to be non significant after removing 5 outlier time points.

It was observed that the scores for FMPS and GIS showed saturation for a large number of patients; 114 out of the 320 measurements were equal to 1 (36 %). Thus, these indices may not have adequate discriminative ability and the non-significant results might be attributed to this factor. However, we consider this unlikely, as the ‘brush’ factor showed no evidence of a significant effect even in the other outcome measures. However, it must be noted that the residuals of the linear models for FMPS and GISwere not normally distributed, and this might have affected the models’ validity.

Conclusions

This 3-month, parallel clinical trial demonstrated that the electric 3D (Oral-B) and the manual (Oral B) orthodontic brushes were equally effective in removing plaque and reducing gingival inflammation in patients undergoing fixed orthodontic treatment. This suggests that further research is necessary to improve the designs of orthodontic toothbrushes. Clinicians should focus onenhancing their patients' dental awareness and oralhygiene along with professional prophylaxis and other oral hygiene aids independently the brush used.

Declaration of interests

There are no competing interests to declare.

References

Ainamo J, Xie Q, Ainamo A, Kallio P. Assessment of the effect of an oscillating/rotating toothbrush on oral health. A 12-month longitudinal study. J Clin Periodontol 1997;24:28-33.

Al-Anezi S, Harradine N. Quantifying plaque during orthodontic treatment: A systematic review. Angle Orthod 2012;82:748-753.

Atak NE, Sandy JR, Addy M. Periodontal and microbiological changes associated with the placement of orthodontic appliances. A review. J Periodontol 1996;67:78-85.

Ay ZY, Sayin, MÖ, Özat Y, Goster, T, Atilla AO, Bozkurt FY. Appropriate oral hygiene motivation method for patients with fixed appliances. Angle Orthod 2007;77:1085-1089.

Bass CC. An effective method of personal oral hygiene. J La State Med Soc 1954;106:100-12

Borutta A, Pala E, Fischer T. Effectiveness of a powered toothbrush compared with a manual toothbrush for orthodontic patients with fixed appliances. J Clin Dent 2002;13:131-7.

Buck T, Pellegrini P, Sauerwein R, Leo MC, Covell DA, Jr Maier T, Machida CA. Elastomeric-ligated vs self-ligating appliances: a pilot study examining microbial colonization and white spot lesion formation after 1 year of orthodontic treatment. Orthodontics: The Art and Practice of Dentofacial Enhancement 2011;12:108-121.

Cardoso MA, Saraiva PP, Maltagliati LA, Rhoden FK, Costa CCA, Normando D, Capelozza Filho L. Alterations in plaque accumulation and gingival inflammation promoted by treatment with self-ligating and conventional orthodontic brackets. Dental Press J Orthod 2015;20:35-41.

Clerehugh V, Williams P, Shaw WC, Worthington HV, Warren P. A practice-based randomised controlled trial of the efficacy of an electric and a manual toothbrush on gingival health in patients with fixed orthodontic appliances. J Dent 1998;26:633-9.

Conforti NJ, Cordero RE, Liebman J, Bowman JP, Putt MS, Kuebler DS, Davidson KR, Cugini M, Warren PR. An investigation into the effect of three months' clinical wear on toothbrush efficacy: results from two independent studies. J Clin Dent 2003;14(2):29-33.

Costa MR, Silva VC, Miqui MN, SakimaT, Spolidorio DM, Cirelli JA. Efficacy of ultrasonic, electric and manual toothbrushes in patients with fixed orthodontic appliances. Angle Orthod 2007;77:361-6.

Costa MR, Silva VC, Miqui MN. Effects of ultrasonic, electric, and manual toothbrushes on subgingival plaque composition in orthodontically banded molars. Am J Orthod Dentofacial Orthop 2010;137:229-235.

Council on Scientific Affairs, American Dental Association. Acceptance program guidelines. Toothbrushes.2012.http://www.ada.org/~/media/ADA/ScienceandResearch/Files/guide_toothbrushes.ashx

D'Costa K, Dana R, Ip G, Kong E, Vol I. Electric versus manual toothbrushes in the fixed orthodontic patient: an evidence-based review. University of Toronto, Faculty of Dentistry, 2011. https://www.dentistry.utoronto.ca/system/files/x1_2011

Erbe C, Klees V, Braunbeck F, Ferrari-Peron P, Ccahuana-Vasquez RA, Timm H,Grender J, Cunningham P, Adam R, Wehrbein H. Comparative assessment of plaque removal and motivation between a manual toothbrush and an interactive power toothbrush in adolescents with fixed orthodontic appliances: A single-center, examiner-blind randomized controlled trial. Am J Orthod Dentofacial Orthop. 2019 Apr;155(4):462-472

Erbe C, Klukowska M, Timm HC, Barker ML, van der Wielen J, Wehrbein H. A randomized controlled trial of a power brush/irrigator/mouthrinse routine on plaque and gingivitis reduction in orthodontic patients. Angle Orthod. 2019 May;89(3):378-384

Hans Timm,b Julie Grender,c Pamela Cunningham,c Ralf Adam,b and Heinrich Wehrbeina

Flemmig TF. Periodontitis. Ann Periodontol 1999:4:32-37.

Heasman P, Wilson Z, Macgregor I, Kelly P. Comparative study of electric and manual toothbrushes in patients with fixed orthodontic appliances. Am J Orthod Dentofacial Orthop 1998;114:45-9.

Hickman J, Millett DT, Sander L , Brown E, Love J. Powered vs manual tooth brushing in fixed appliance patients: A short term randomized clinical trial. Angle Orthod 2002;72:135-40.

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.

Hogan LM, Daly CG, Curtis BH. Comparison of new and 3-month-old brush heads in the removal of plaque using a powered toothbrush. J Clin Periodontol 2007;34:130-6.

Huang GJ. Insufficient evidence to conclude that orthodontic patients derive benefits from using power toothbrushes. JADA 2009;140:914-915.

Kaklamanos EG, Kalfas S. Meta-analysis on the effectiveness of powered toothbrushes for orthodontic patients. Am J Orthod Dentofacial Orthop 2008;133:187.e1-14.

Klukowska M, Bader A, Erbe C, Bellamy P, White D, Anastasia M, Wehrbeing H. Plaque levels of patients with fixed orthodontic appliances measured by digital plaque image analysis. Am J Orthod Dentofacial Orthop 2011;139:463-470

Kreifeldt JG, Hill PH, Calisti LJ. A systematic study of the plaque removal efficiency of worn toothbrushes. J Dent Res 1980;59:2047-55.

Lindhe J. Textbook of Clinical Periodontology. 1st Edition. Coopenhagen. Munskgaard. 1981.

Löe H, Silness J. Periodontal Disease in Pregnancy I. Prevalence and Severity. Acta Odontologica Scandinavica 1963;21:533-551

Löe H. The gingival index, the plaque index and the retention index systems. J Periodontol 1967;38:610-6.

Al Makhmari SA, Kaklamanos EG, Athanasiou AE. Short-term and long-termeffectiveness of powered toothbrushes in promoting periodontal health duringorthodontic treatment: A systematic review and meta-analysis. Am J OrthodDentofacial Orthop. 2017 Dec;152(6):753-766.e7.

Mariotti A. Dental plaque-induced gingival diseases. Ann Periodontol 1999;4:7-19.

Makhmari S., Kaklamanos E., Athanasiou A.Am J Orthod Dentofacial Orthop 2017;;152:753-66

O'Leary TJ, Drake RB, Naylor JE. The plaque control record. J Periodontol 1972;43:38.

Robinson PG, Walmsley AD, 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;77:1944-1953.

Silness J, Löe H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. Acta Odontologica Scandinavica 1964;22:121-135.

Tan E, Daly C. Comparison of new and 3-month-old toothbrushes in plaque removal. J Clin Periodontol 2002;29:645-50.

Tangade PS, Shah AF, Ravishankar TL, Tirth A, Pal S. Is plaque removal efficacy of toothbrush related to bristle flaring? A 3-month prospective parallel experimental study. Ethiop J Health Sci 2013;23:255-64.

Thienpont V, Dermaut L R, Van Maele G. Comparative study of 2 electric and 2 manual toothbrushes in patients with fixed orthodontic appliances. Am J Orthod and Dentofacial Orthop 2001;120:353-360.

Trimpeneers LM, Wijgaerts IA, Grognard NA,Dermaut LR, Adriaens PA. Effect of electric toothbrushes versus manual toothbrushes on removal of plaque and periodontal status during orthodontic treatment. Am J Orthod Dentofacial Orthop 1997;111:492-497.

Türkkahraman H, Sayin MO, Bozkurt FY, Yetkin Z, Kaya S, Onal S. Archwire ligation techniques, microbial colonization, and periodontal status in orthodontically treated patients. Angle Orthod 2005;75:231-6.

Van der Weijden GA, Timmerman MF, Nijboer A, Lie MA, Van der Velden U. A comparative study of electric toothbrushes for the effectiveness of plaque removal in relation to toothbrushing duration. Timerstudy. J Clin Periodontol 1993;20:476-81.

Van der Weijden F., Echeverría J.J., Sanz M., Lindhe J. Mechanical Supragingival Plaque Control. In Lindhe J., Lang N. P. and Thorkild K. “Clinical Periodontology and Implant Dentistry”. Fifth Edition. Blackwell Munksgaard Publishing Company. 2008. Chapter 35, pages 705-733.

Warren PR, Chater B. The role of the electric toothbrush in the control of plaque and gingivitis: a review of 5 years clinical experience with the Braun Oral-B Plaque Remover (D7). Am J Dent. 1996; 9 Spec No:5–11.

Williams P, Clerehugh V, Worthington HV, Shaw WC. Comparison of two plaque indices for use in fixed orthodontic appliance patients. J Dent Res 1991;70:703. Abstract 276.

Yaacob M, Worthington HV, Deacon SA, Deery C, Walmsley AD, Robinson PG, Glenny AM. Powered versus manual toothbrushing for oral health. Cochrane Database of Systematic Reviews 2014, Issue 6.

Tables

Table 1 Values of PIM index

0	No plaque
1	A film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may be seen in situ only after application of disclosing solution or by using the probe on the tooth surface.
2	Moderate accumulation of soft deposits within the gingival pocket, or the tooth and gingival margin which can be seen with the naked eye.
3	Abundance of soft matter within the gingival pocket and/or on the tooth and gingival margin.

Table 2 Values of GI index

0	normal gingiva
1	mild inflammation, slight change in colour and subtle change in texture, no bleeding on probing the gingival crest
2	moderate inflammation, moderate glazing, redness, oedema, bleeding on probing the gingival crest
3	severe inflammation, marked redness and oedema/enlargement, ulceration, bleeding on probing the gingival crest and/or spontaneously

Table 3 Participant Timeline

	T0	T1	T2	T3
PI-M	+	+	+	+
FMPS-M	+	+	+	+
GI-M	+	+	+	+
GI-SM	+	+	+	+
Give brushes				+

Table 4 Sample effect size Klukowska et al. (2011)

Difference in means(%)	Sample size (per group)
10	126
15	57
20	33
30	15
40	9

Table 5 Sample effect size Clerehugh et al. (1998)

Difference in means (%)	Sample size (per group)
10	92
15	42
20	24
30	12
40	7

Table 6 Descriptive statistics

	Electric (n = 40)			Manual (n = 40)	
	Average (SD) or Count (%)	Median (IQR*)		Average (SD) or Count (%)	Median (IQR*)
Sex (female)	20 (50%)			20 (50%)	
T0 (Baseline):					
Age (years)	14.3 (1.43)	14.08 (2.11)		13.8 (1.55)	13.75 (2.20)
PIM	0.31 (0.10)	0.30 (0.14)		0.32 (0.11)	0.32 (0.17)
FMPS	0.92 (0.14)	0.97 (0.12)		0.91 (0.14)	0.97 (0.10)
GI	0.62 (0.13)	0.67 (0.23)		0.62 (0.13)	0.64 (0.21)
GIS	0.92 (0.16)	1.00 (0.10)		0.91 (0.14)	1.00 (0.16)
T1:					
T1-T0 (days)	31.8 (14.92)	28.0 (2.0)		34.5 (13.53)	33.0 (8.3)
PIM	0.29 (0.10)	0.27 (0.15)		0.30 (0.10)	0.29 (0.12)
FMPS	0.89 (0.14)	0.95 (0.15)		0.89 (0.14)	0.95 (0.15)
GI	0.61 (0.12)	0.59 (0.16)		0.63 (0.12)	0.66 (0.14)
GIS	0.92 (0.13)	1.00 (0.11)		0.92 (0.15)	1.00 (0.08)
T2:					
T2-T1 (days)	33.7 (15.80)	28.0 (14.0)		30.3 (11.99)	28.0 (10.3)
PIM	0.29 (0.09)	0.27 (0.13)		0.29 (0.07)	0.29 (0.08)
FMPS	0.91 (0.12)	0.95 (0.11)		0.91 (0.11)	0.95 (0.12)
GI	0.60 (0.12)	0.61 (0.15)		0.63 (0.11)	0.64 (0.11)
GIS	0.90 (0.16)	1.00 (0.17)		0.92 (0.12)	0.97 (0.10)
T3:					
T3-T2 (days)	30.2 (9.44)	28.0 (14.0)		31.9 (11.47)	28.5 (20.3)
PIM	0.29 (0.10)	0.28 (0.10)		0.29 (0.08)	0.29 (0.11)
FMPS	0.92 (0.12)	0.97 (0.10)		0.92 (0.10)	0.95 (0.10)
GI	0.62 (0.13)	0.64 (0.14)		0.62 (0.10)	0.64 (0.12)
GIS	0.91 (0.15)	1.00 (0.15)		0.92 (0.14)	1.00 (0.11)

*IQR: Interquartile range

Figures

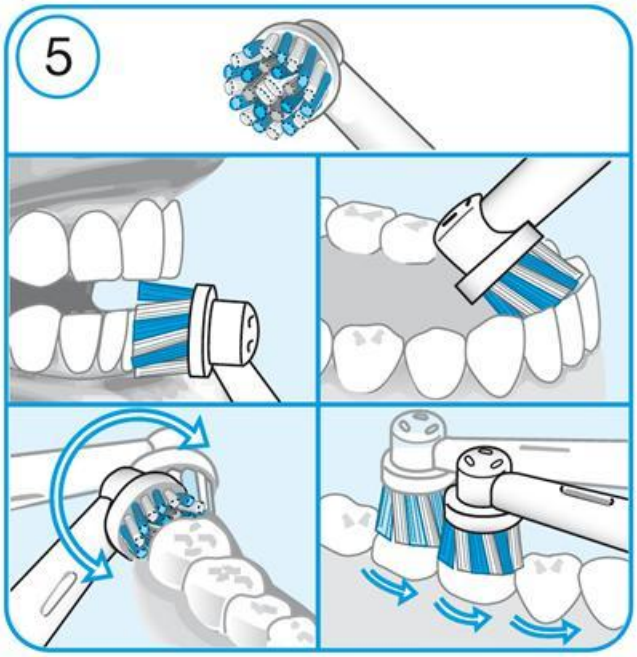

Figure 1. Brushing instructions. From: Oral-B Tri-zone 500-5000, document 97253545/IV-15

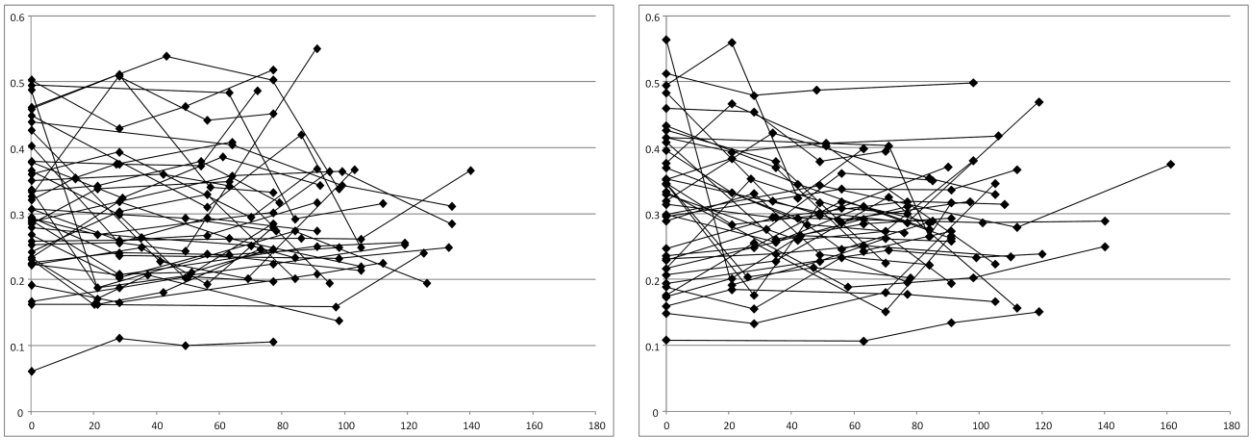

Figure 2. Plots of PIM profiles over time for the 40 individuals of each group (Electric and Manual). Time is in days from baseline.

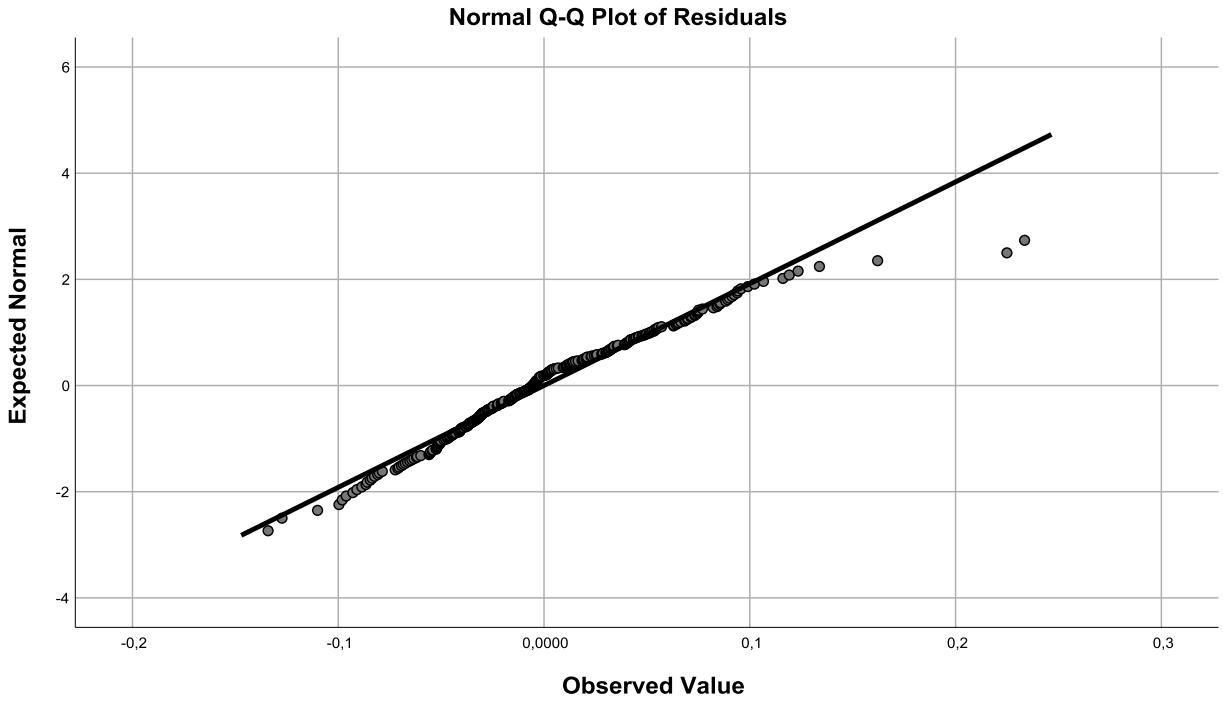

Figure 3 Q-Q plot of the residuals of Model PIM-5.

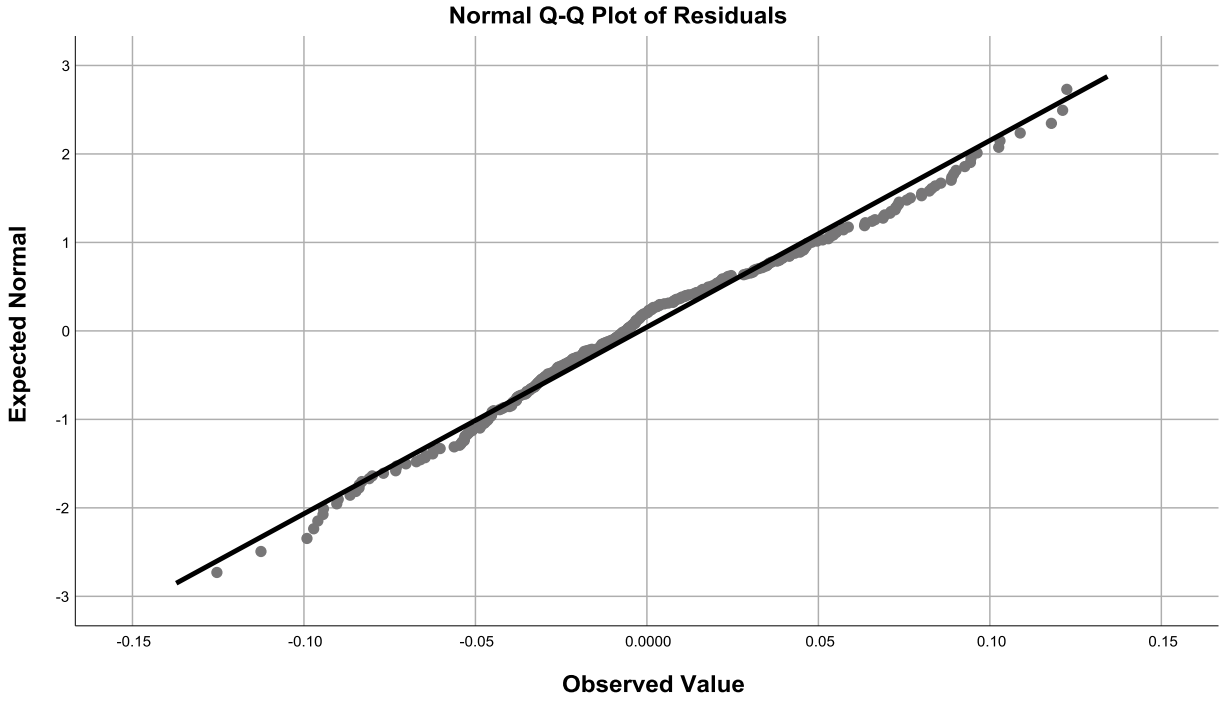

Figure 4 Q-Q plot of the residuals of Model PIM-7.

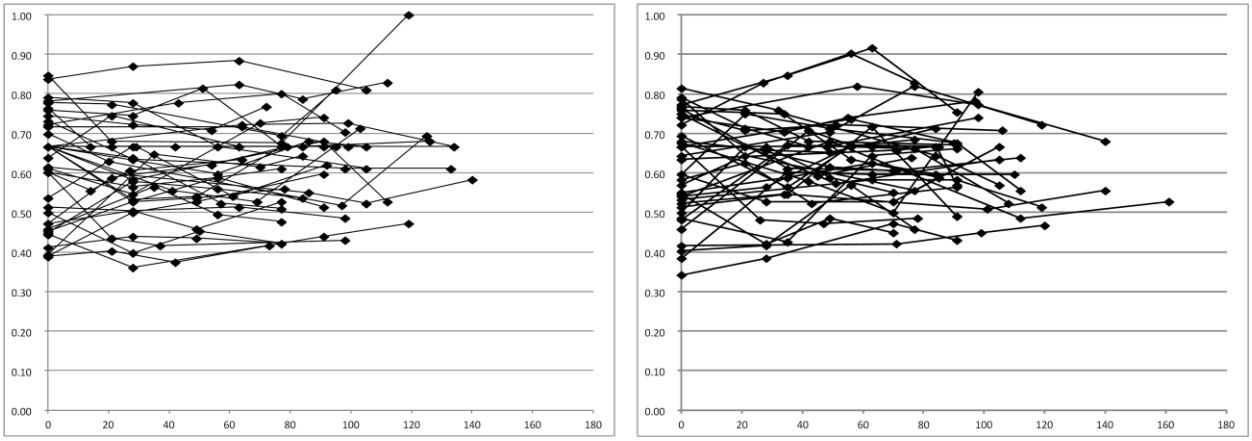

Figure 5 Plots of GI profiles over time for the 40 individuals of each group (Electric and Manual). Time is in days from baseline

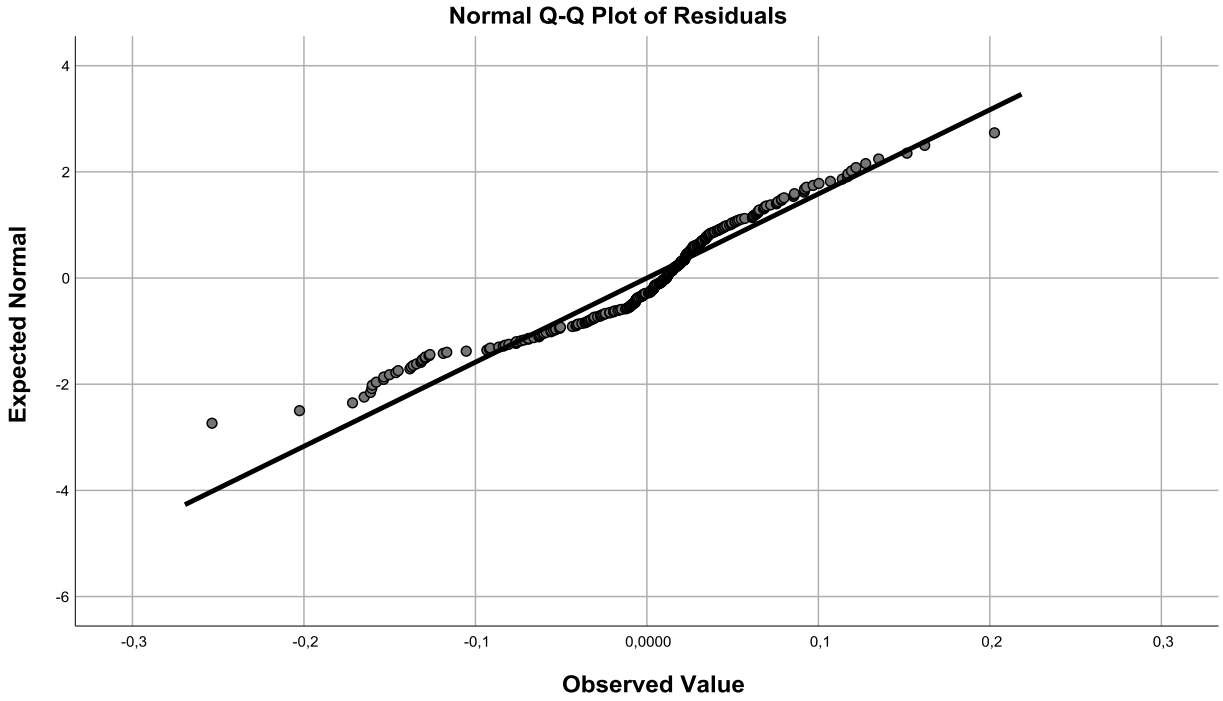

Figure 6 Q-Q plot of the residuals of Model GI-5.

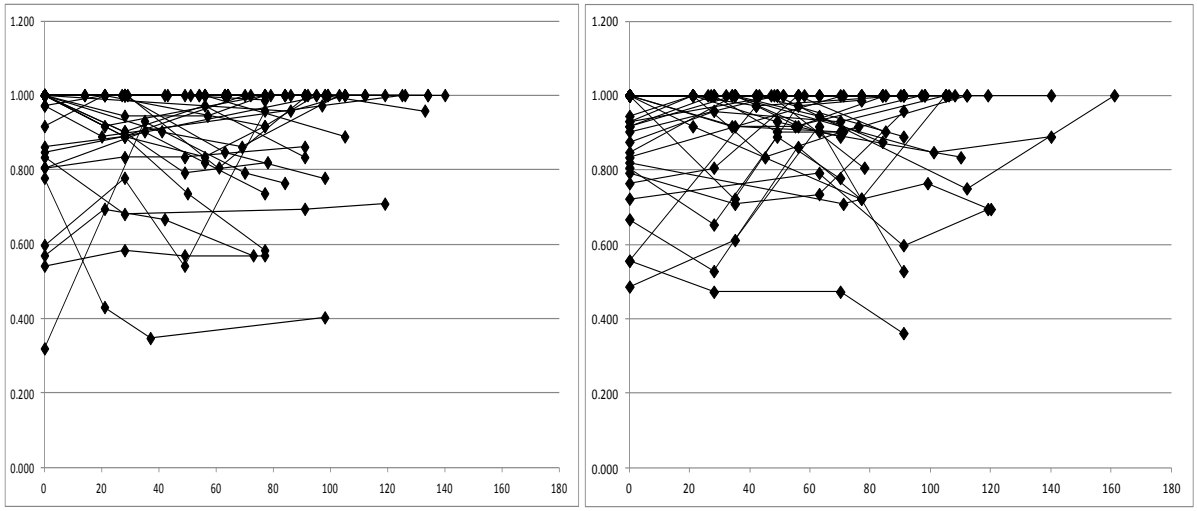

Figure 7 Plots of FMPS profiles over time for the 40 individuals of each group (Electric and Manual). Time is in days from baseline.

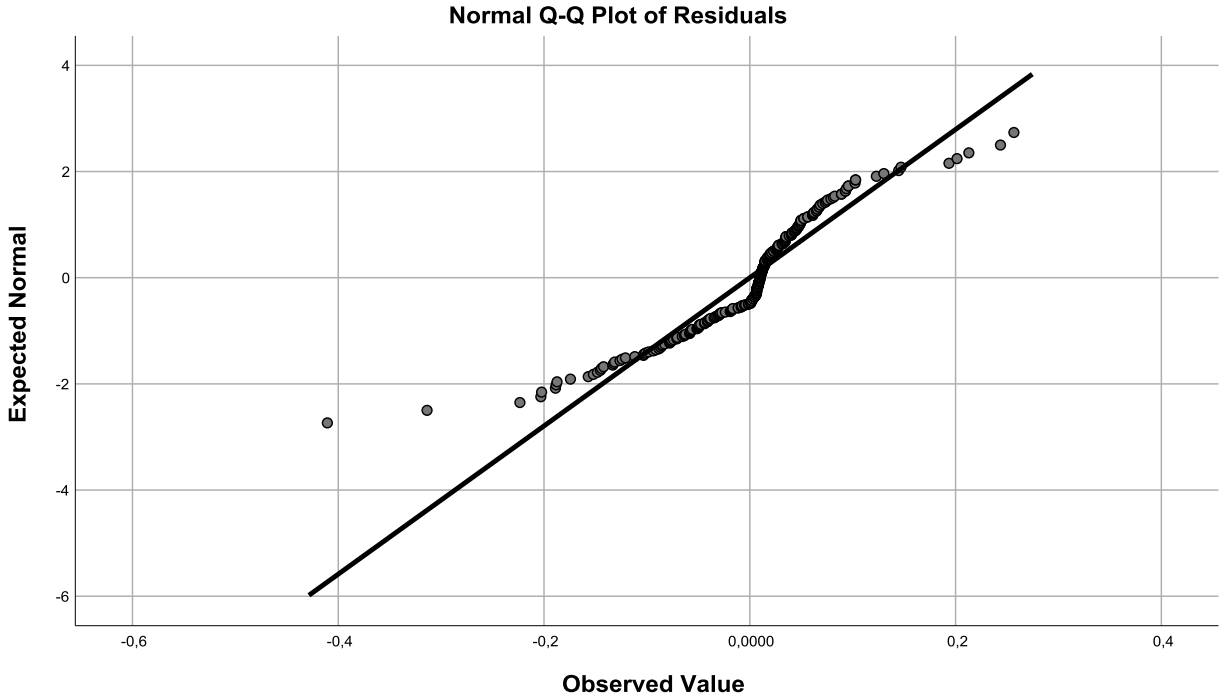

Figure 8 Q-Q plot of the residuals of Model FMPS-6.

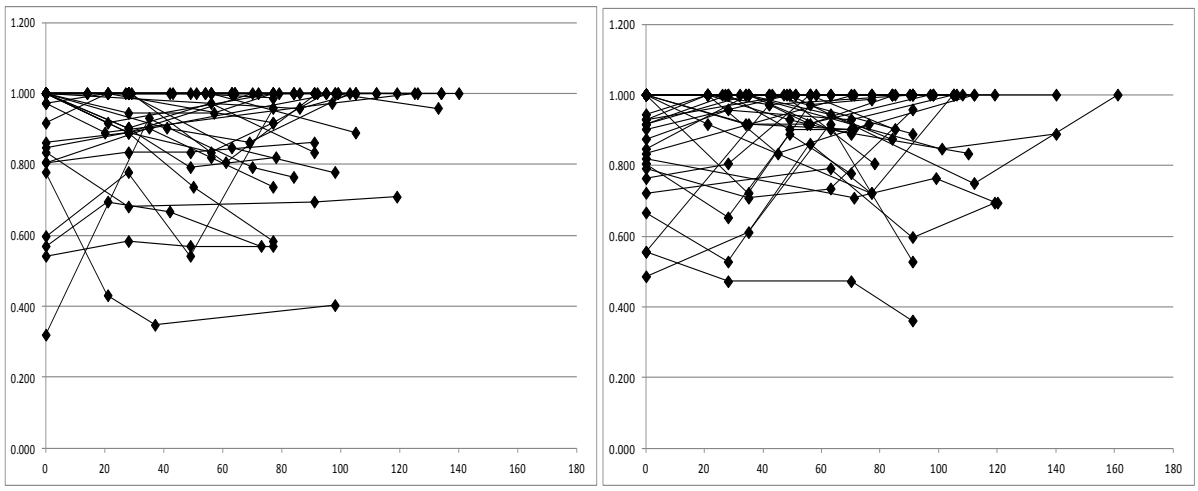

Figure 9 Plots of GIS profiles over time for the 40 individuals of each group (Electric and Manual). Time is in days from baseline.

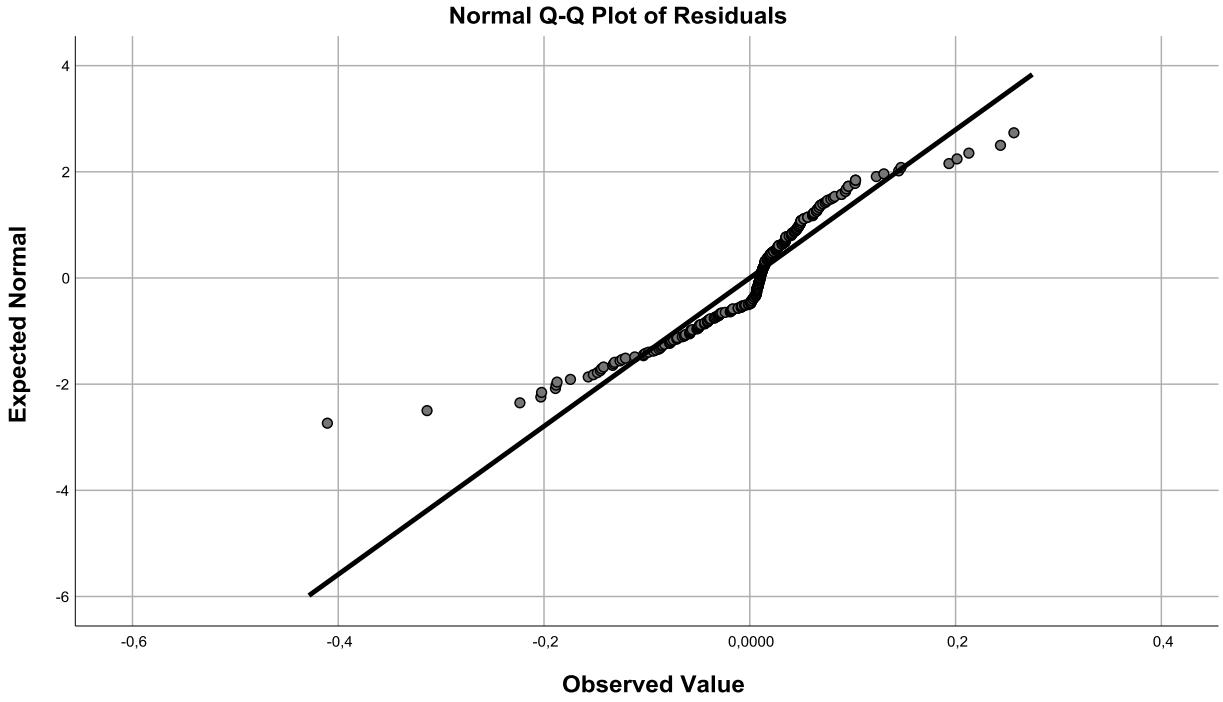

Figure 10 Q-Q plot of the residuals of Model GIS

Supplementary text

Model PIM-1 - Unconditional mean model

SPSS syntax

```
MIXED pim
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=| SSTYPE(3)
  /METHOD=ML
  /PRINT=SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN)
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		2		3	
a. Dependent Variable: pim .					

Information Criteria[a]	
-2 Log Likelihood	-723.213
Akaike's Information Criterion (AIC)	-717.213
Hurvich and Tsai's Criterion (AICC)	-717.137
Bozdogan's Criterion (CAIC)	-702.908
Schwarz's Bayesian Criterion (BIC)	-705.908

The information criteria are displayed in smaller-is-better form.
a. Dependent Variable: pim .

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	80	1186.057	.000
a. Dependent Variable: pim .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.297931	.008651	80	34.439	.000	.280715	.315147
a. Dependent Variable: pim .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.003875	.000354	10.954	.000	.003240	.004634
Intercept [subject = patientid]	Variance	.005018	.000951	5.278	.000	.003462	.007275
a. Dependent Variable: pim .							

ICC = 0.005018 / (0.005018 + 0.003875) = 0.56.

Model PIM-2 - Linear time

Time (scaled to months from baseline) was entered into the model both as a fixed and a random variable.

SPSS Syntax

```
MIXED pim WITH dt_m
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=dt_m | SSTYPE(3)
  /METHOD=ML
/PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	dt_m	1		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		4		6	
a. Dependent Variable: pim .					
b. As of version 11.5, the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax, please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-736.843
Akaike's Information Criterion (AIC)	-724.843
Hurvich and Tsai's Criterion (AICC)	-724.574
Bozdogan's Criterion (CAIC)	-696.233
Schwarz's Bayesian Criterion (BIC)	-702.233

The information criteria are displayed in smaller-is-better form.
a. Dependent Variable: pim .

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	78.782	774.396	.000
dt_m	1	55.464	4.877	.031
a. Dependent Variable: pim .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.308337	.011080	78.782	27.828	.000	.286282	.330392
dt_m	-.006678	.003024	55.464	-2.208	.031	-.012737	-.000619
a. Dependent Variable: pim .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.003469	.000398	8.710	.000	.002770	.004345
Intercept + dt_m [subject = patientid]	UN (1,1)	.007498	.001589	4.720	.000	.004950	.011358
	UN (2,1)	-.000903	.000390	-2.315	.021	-.001668	-.000139
	UN (2,2)	.000173	.000140	1.232	.218	3.525124E-5	.000849
a. Dependent Variable: pim .							

Random Effect Covariance Structure (G)[a]

	Intercept | patientid	dt_m | patientid
Intercept | patientid	.007498	-.000903
dt_m | patientid	-.000903	.000173
Unstructured		
a. Dependent Variable: pim .		

The linear model shows that there is significant difference in slopes between patients. The residual variance (Residual estimate of the covariance parameters) declined from .003875 (Model 1) to .003469 (difference of .000406, or 10.5%).The correlation of the intercept with the linear growth parameter was negative (-.000903, p=.021) so patients with a high PIM had a slower decrease than patients with a low PIM.

Model PIM-3 - brush, time, time * brush

Brush and time * brush interaction were added to the model.

SPSS Syntax

```
MIXED pim BY brush WITH dt_m
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=dt_m brush brush*dt_m | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	dt_m	1		1	

	brush	2		1	
	brush * dt_m	2		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		8		8	
a. Dependent Variable: pim .					
b. As of version 11.5, the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax, please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-736.866
Akaike's Information Criterion (AIC)	-720.866
Hurvich and Tsai's Criterion (AICC)	-720.403
Bozdogan's Criterion (CAIC)	-682.720
Schwarz's Bayesian Criterion (BIC)	-690.720
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: pim .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	78.753	774.186	.000
dt_m	1	54.363	4.865	.032
brush	1	78.753	.001	.971
brush * dt_m	1	54.363	.019	.891
a. Dependent Variable: pim .				

Estimates of Fixed Effects[a]						
Parameter	Estimate	Std. Error	df	t	Sig.	95% Confidence Interval

						Lower Bound	Upper Bound
Intercept	.307945	.015648	78.266	19.680	.000	.276794	.339096
dt_m	-.006270	.004278	53.671	-1.466	.149	-.014847	.002308
[brush=0]	.000808	.022164	78.753	.036	.971	-.043311	.044926
[brush=1]	0[b]	0	.	.	.	.	.
[brush=0] * dt_m	-.000831	.006062	54.363	-.137	.891	-.012983	.011320
[brush=1] * dt_m	0[b]	0	.	.	.	.	.
a. Dependent Variable: pim .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.003462	.000400	8.662	.000	.002761	.004341
Intercept + dt_m [subject = patientid]	UN (1,1)	.007505	.001590	4.720	.000	.004955	.011368
	UN (2,1)	-.000909	.000393	-2.315	.021	-.001678	-.000139
	UN (2,2)	.000177	.000143	1.237	.216	3.625098E-5	.000862
a. Dependent Variable: pim .							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.007505	-.000909
dt_m | patientid	-.000909	.000177
Unstructured		
a. Dependent Variable: pim .		

Model PIM-4 - Full model

SPSS Syntax

```
MIXED pim BY brush sexn WITH dt_m age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=brush sexn dt_m age_c brush*sexn brush*dt_m brush*age_c sexn*dt_m sexn*age_c dt_m*age_c |
    SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	brush	2		1	
	sexn	2		1	
	dt_m	1		1	
	age_c	1		1	
	brush * sexn	4		1	
	brush * dt_m	2		1	
	brush * age_c	2		1	
	sexn * dt_m	2		1	
	sexn * age_c	2		1	
	dt_m * age_c	1		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		22		15	

a. Dependent Variable: pim .

b. As of version 11.5, the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax, please consult the current syntax reference guide for more information.

Information Criteria[a]	
-2 Log Likelihood	-750.837
Akaike's Information Criterion (AIC)	-720.837
Hurvich and Tsai's Criterion (AICC)	-719.258
Bozdogan's Criterion (CAIC)	-649.312
Schwarz's Bayesian Criterion (BIC)	-664.312
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: pim .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	81.369	850.760	.000
brush	1	76.981	.165	.686
sexn	1	77.325	8.093	.006
dt_m	1	46.944	6.215	.016
age_c	1	77.361	5.257	.025
brush * sexn	1	76.016	2.685	.105
brush * dt_m	1	41.705	.016	.899
brush * age_c	1	78.473	.403	.527
sexn * dt_m	1	43.091	6.374	.015
sexn * age_c	1	78.240	.364	.548
dt_m * age_c	1	38.743	2.385	.131
a. Dependent Variable: pim .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound

Intercept	.269844	.019414	86.249	13.900	.000	.231252	.308436
[brush=0]	.017960	.026618	99.341	.675	.501	-.034853	.070772
[brush=1]	0[b]	0	.	.	.	.	.
[sexn=0]	.087089	.026713	96.323	3.260	.002	.034067	.140111
[sexn=1]	0[b]	0	.	.	.	.	.
dt_m	-9.750740E-5	.004793	36.095	-.020	.984	-.009817	.009622
age_c	-.023400	.010955	96.478	-2.136	.035	-.045144	-.001655
[brush=0] * [sexn=0]	-.052894	.032277	76.016	-1.639	.105	-.117179	.011391
[brush=0] * [sexn=1]	0[b]	0	.	.	.	.	.
[brush=1] * [sexn=0]	0[b]	0	.	.	.	.	.
[brush=1] * [sexn=1]	0[b]	0	.	.	.	.	.
[brush=0] * dt_m	.000740	.005813	41.705	.127	.899	-.010993	.012473
[brush=1] * dt_m	0[b]	0	.	.	.	.	.
[brush=0] * age_c	.006985	.011001	78.473	.635	.527	-.014913	.028884
[brush=1] * age_c	0[b]	0	.	.	.	.	.
[sexn=0] * dt_m	-.014940	.005917	43.091	-2.525	.015	-.026873	-.003007
[sexn=1] * dt_m	0[b]	0	.	.	.	.	.
[sexn=0] * age_c	.006626	.010989	78.240	.603	.548	-.015250	.028501
[sexn=1] * age_c	0[b]	0	.	.	.	.	.
dt_m * age_c	.003134	.002029	38.743	1.544	.131	-.000971	.007239
a. Dependent Variable: pim .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]							
Parameter		Estimate	Std. Error	Wald Z	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Residual		.003535	.000424	8.330	.000	.002794	.004473
Intercept + dt_m [subject = patientid]	UN (1,1)	.006078	.001397	4.350	.000	.003873	.009537
	UN (2,1)	-.000651	.000360	-1.809	.070	-.001356	5.438503E-5
	UN (2,2)	9.868394E-5	.000144	.686	.493	5.670391E-6	.001717

a. Dependent Variable: pim .

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.006078	-.000651
dt_m | patientid	-.000651	9.868394E-5
Unstructured		
a. Dependent Variable: pim .		

Model PIM-5 - Main effects and sex * time

SPSS Syntax

```
MIXED pim BY brush sexn WITH dt_m age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=brush sexn dt_m age_c sexn*dt_m | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	brush	2		1	
	sexn	2		1	
	dt_m	1		1	
	age_c	1		1	
	sexn * dt_m	2		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid

Residual			1	
Total	11		10	
a. Dependent Variable: pim .				
b. As of version 11.5, the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax, please consult the current syntax reference guide for more information.				

Information Criteria[a]	
-2 Log Likelihood	-745.174
Akaike's Information Criterion (AIC)	-725.174
Hurvich and Tsai's Criterion (AICC)	-724.462
Bozdogan's Criterion (CAIC)	-677.491
Schwarz's Bayesian Criterion (BIC)	-687.491
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: pim .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	76.658	877.725	.000
brush	1	77.734	.122	.727
sexn	1	79.568	6.855	.011
dt_m	1	54.156	5.887	.019
age_c	1	77.337	2.938	.091
sexn * dt_m	1	54.365	4.744	.034
a. Dependent Variable: pim .				

Estimates of Fixed Effects[a]						
Parameter	Estimate	Std. Error	df	t	Sig.	95% Confidence Interval

						Lower Bound	Upper Bound
Intercept	.283963	.016746	89.099	16.957	.000	.250690	.317236
[brush=0]	-.005658	.016165	77.734	-.350	.727	-.037841	.026526
[brush=1]	0[b]	0	.	.	.	.	.
[sexn=0]	.055878	.021342	79.568	2.618	.011	.013403	.098353
[sexn=1]	0[b]	0	.	.	.	.	.
dt_m	-.000722	.003913	39.619	-.185	.854	-.008634	.007189
age_c	-.009580	.005589	77.337	-1.714	.091	-.020708	.001548
[sexn=0] * dt_m	-.012698	.005830	54.365	-2.178	.034	-.024384	-.001012
[sexn=1] * dt_m	0[b]	0	.	.	.	.	.
a. Dependent Variable: pim .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.003530	.000409	8.642	.000	.002814	.004429
Intercept + dt_m [subject = patientid]	UN (1,1)	.006333	.001439	4.403	.000	.004058	.009885
	UN (2,1)	-.000655	.000358	-1.827	.068	-.001357	4.769046E-5
	UN (2,2)	.000109	.000135	.806	.420	9.554447E-6	.001238
a. Dependent Variable: pim .							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.006333	-.000655
dt_m | patientid	-.000655	.000109
Unstructured		
a. Dependent Variable: pim .		

Model PIM-6 - sex, time, sex * time

SPSS Syntax

```
MIXED pim BY sexn WITH dt_m
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=sexn dt_m sexn*dt_m | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	sexn	2		1	
	dt_m	1		1	
	sexn * dt_m	2		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		8		8	
a. Dependent Variable: pim .					
b. As of version 11.5, the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax, please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-742.417
Akaike's Information Criterion (AIC)	-726.417
Hurvich and Tsai's Criterion (AICC)	-725.954
Bozdogan's Criterion (CAIC)	-688.271
Schwarz's Bayesian Criterion (BIC)	-696.271

The information criteria are displayed in smaller-is-better form.
a. Dependent Variable: pim .

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	78.031	828.715	.000
sexn	1	78.031	5.067	.027
dt_m	1	51.575	5.876	.019
sexn * dt_m	1	51.575	4.788	.033
a. Dependent Variable: pim .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.284457	.015144	77.642	18.783	.000	.254305	.314609
[sexn=0]	.048259	.021439	78.031	2.251	.027	.005577	.090940
[sexn=1]	0[b]	0	.	.	.	.	.
dt_m	-.000683	.003876	36.717	-.176	.861	-.008539	.007174
[sexn=0] * dt_m	-.012664	.005787	51.575	-2.188	.033	-.024279	-.001048
[sexn=1] * dt_m	0[b]	0	.	.	.	.	.
a. Dependent Variable: pim .							
b. This parameter is set to zero because it is redundant.							

Bootstrap for Estimates of Fixed Effects						
		Bootstrap[a]				
					95% Confidence Interval	
Parameter	Estimate	Bias	Std. Error	Sig. (2-tailed)	Lower	Upper
Intercept	.284457	-.001066	.008202	.000	.266809	.298828
[sexn=0]	.048259	4.845573E-5	.013136	.000	.022127	.074375

[sexn=1]	0	0	0		0	0
dt_m	-.000683	-.001190	.004144	.799	-.009859	.006373
[sexn=0] * dt_m	-.012664	.002180	.006546	.008	-.023193	.002248
[sexn=1] * dt_m	0	0	0		0	0
a. Unless otherwise noted, bootstrap results are based on 10000 bootstrap samples						

Covariance Parameters

Estimates of Covariance Parameters[a]							
Parameter		Estimate	Std. Error	Wald Z	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Residual		.003557	.000417	8.521	.000	.002826	.004477
Intercept + dt_m [subject = patientid]	UN (1,1)	.006813	.001503	4.533	.000	.004421	.010499
	UN (2,1)	-.000719	.000366	-1.963	.050	-.001437	-1.281694E-6
	UN (2,2)	.000100	.000136	.736	.462	6.997776E-6	.001437
a. Dependent Variable: pim .							

Bootstrap for Estimates of Covariance Parameters							
Parameter		Estimate	Bootstrap[a]				
			Bias	Std. Error	Sig. (2-tailed)	95% Confidence Interval	
						Lower	Upper
Residual		.003557	-.002002	.000344	.792	.000949	.002268
Intercept + dt_m [subject = patientid]	UN (1,1)	.006813	.003373	.001336	.000	.007908	.013117
	UN (2,1)	-.000719	-.001423	.000547	.710	-.003384	-.001247
	UN (2,2)	.000100	.000889	.000315	1.000	.000493	.001664
a. Unless otherwise noted, bootstrap results are based on 10000 bootstrap samples							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.006813	-.000719
dt_m | patientid	-.000719	.000100

Unstructured
a. Dependent Variable: pim .

Model comparison

Information Criteria	Model PIM-2 (linear time)	Model PIM-3 (brush, time, time * brush)	Model PIM-4 (main effects and 2-way interactions)	Model PIM-5 (main effects and sex * time)	Model PIM-6 (sex, time, sex * time)
-2 Log Likelihood	-736.843	-736.866	**-750.837**	-745.174	-742.417
Akaike's Information Criterion (AIC)	-724.843	-720.866	-720.837	-725.174	**-726.417**
Hurvich and Tsai's Criterion (AICC)	-724.574	-720.403	-719.258	-724.462	**-725.954**
Bozdogan's Criterion (CAIC)	**-696.233**	-682.720	-649.312	-677.491	-688.271
Schwarz's Bayesian Criterion (BIC)	**-702.233**	-690.720	-664.312	-687.491	-696.271

The information criteria are displayed in smaller-is-better form.

Bold values indicate the better model.

Model PIM-7 - sex, time, sex * time - 5 outliers removed

SPSS Syntax

```
MIXED pim BY sexn WITH dt_m
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=sexn dt_m sexn*dt_m | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]

		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	sexn	2		1	
	dt_m	1		1	
	sexn * dt_m	2		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		8		8	
a. Dependent Variable: pim .					
b. As of version 11.5, the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax, please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-793.648
Akaike's Information Criterion (AIC)	-777.648
Hurvich and Tsai's Criterion (AICC)	-777.177
Bozdogan's Criterion (CAIC)	-739.627
Schwarz's Bayesian Criterion (BIC)	-747.627
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: pim .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	78.555	784.261	.000
sexn	1	78.555	2.915	.092
dt_m	1	62.119	6.331	.014

sexn * dt_m	1	62.119	1.182	.281
a. Dependent Variable: pim .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.286869	.015368	77.545	18.667	.000	.256271	.317468
[sexn=0]	.037251	.021817	78.555	1.707	.092	-.006179	.080681
[sexn=1]	0[b]	0	.	.	.	.	.
dt_m	-.003879	.003662	47.405	-1.059	.295	-.011245	.003487
[sexn=0] * dt_m	-.005900	.005428	62.119	-1.087	.281	-.016751	.004950
[sexn=1] * dt_m	0[b]	0	.	.	.	.	.
a. Dependent Variable: pim .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.002628	.000299	8.784	.000	.002103	.003285
Intercept + dt_m [subject = patientid]	UN (1,1)	.007687	.001533	5.014	.000	.005200	.011364
	UN (2,1)	-.000918	.000339	-2.709	.007	-.001582	-.000254
	UN (2,2)	.000148	.000106	1.394	.163	3.629065E-5	.000604
a. Dependent Variable: pim .							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.007687	-.000918
dt_m | patientid	-.000918	.000148
Unstructured		

a. Dependent Variable: pim .

Model PIM-8 - Identical to Model PIM-2 - 5 outliers removed

SPSS Syntax

```
MIXED pim WITH dt_m
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=dt_m | SSTYPE(3)
  /METHOD=ML
/PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	dt_m	1		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		4		6	
a. Dependent Variable: pim .					
b. As of version 11.5, the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax, please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-790.786
Akaike's Information Criterion (AIC)	-778.786
Hurvich and Tsai's Criterion (AICC)	-778.513

Bozdogan's Criterion (CAIC)	-750.270
Schwarz's Bayesian Criterion (BIC)	-756.270
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: pim .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	79.104	753.912	.000
dt_m	1	62.812	6.116	.016
a. Dependent Variable: pim .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.305397	.011123	79.104	27.457	.000	.283259	.327536
dt_m	-.006755	.002732	62.812	-2.473	.016	-.012214	-.001296
a. Dependent Variable: pim .							

Bootstrap for Estimates of Fixed Effects						
		Bootstrap[a]				
					95% Confidence Interval	
Parameter	Estimate	Bias	Std. Error	Sig. (2-tailed)	Lower	Upper
Intercept	.305397	7.826985E-5	.005850	.000	.294011	.316812
dt_m	-.006755	-.000378	.002841	.000	-.012693	-.001583
a. Unless otherwise noted, bootstrap results are based on 10000 bootstrap samples						

Covariance Parameters

Estimates of Covariance Parameters[a]

Parameter		Estimate	Std. Error	Wald Z	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Residual		.002614	.000293	8.918	.000	.002098	.003256
Intercept + dt_m [subject = patientid]	UN (1,1)	.008081	.001584	5.100	.000	.005502	.011867
	UN (2,1)	-.000984	.000346	-2.840	.005	-.001663	-.000305
	UN (2,2)	.000163	.000104	1.557	.120	4.617262E-5	.000573
a. Dependent Variable: pim .							

Bootstrap for Estimates of Covariance Parameters							
Parameter		Estimate	Bootstrap[a]				
			Bias	Std. Error	Sig. (2-tailed)	95% Confidence Interval	
						Lower	Upper
Residual		.002614	-.001413	.000224	.694	.000784	.001658
Intercept + dt_m [subject = patientid]	UN (1,1)	.008081	.002602	.001291	.000	.008488	.013551
	UN (2,1)	-.000984	-.001014	.000483	.016	-.003074	-.001185
	UN (2,2)	.000163	.000614	.000217	.990	.000428	.001269
a. Unless otherwise noted, bootstrap results are based on 10000 bootstrap samples							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.008081	-.000984
dt_m | patientid	-.000984	.000163
Unstructured		
a. Dependent Variable: pim .		

Model comparison

Information Criteria	Model PIM-7 (sex, time, sex * time)	Model PIM-8 (linear time)
-2 Log Likelihood	**-793.648**	-790.786
Akaike's Information Criterion (AIC)	-777.648	**-778.786**

Hurvich and Tsai's Criterion (AICC)	-777.177	**-778.513**
Bozdogan's Criterion (CAIC)	-739.627	**-750.270**
Schwarz's Bayesian Criterion (BIC)	-747.627	**-756.270**

The information criteria are displayed in smaller-is-better form.

Bold values indicate the better model.

Model GI-1 - Unconditional mean model

SPSS Syntax

```
MIXED gi
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=| SSTYPE(3)
  /METHOD=ML
  /PRINT=SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]

		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		2		3	

a. Dependent Variable: gi .

Information Criteria[a]	
-2 Log Likelihood	-634.572
Akaike's Information Criterion (AIC)	-628.572
Hurvich and Tsai's Criterion (AICC)	-628.496
Bozdogan's Criterion (CAIC)	-614.267

Schwarz's Bayesian Criterion (BIC)	-617.267
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: gi .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	80	2946.082	.000
a. Dependent Variable: gi .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.619884	.011421	80	54.278	.000	.597157	.642612
a. Dependent Variable: gi .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.004658	.000425	10.954	.000	.003895	.005571
Intercept [subject = patientid]	Variance	.009270	.001653	5.607	.000	.006535	.013149
a. Dependent Variable: gi .							

ICC = 0.009270 / (0.004658 + 0.009270) = 0.67.

Model GI-2 - Linear time

Time (scaled to months from baseline) was entered into the model both as a fixed and a random variable.

SPSS Syntax

```
MIXED gi WITH dt_m
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=dt_m | SSTYPE(3)
  /METHOD=ML
/PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	dt_m	1		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		4		6	
a. Dependent Variable: gi .					
b. As of version 11.5, the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax, please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-637.815
Akaike's Information Criterion (AIC)	-625.815
Hurvich and Tsai's Criterion (AICC)	-625.546
Bozdogan's Criterion (CAIC)	-597.205
Schwarz's Bayesian Criterion (BIC)	-603.205

The information criteria are displayed in smaller-is-better form.
a. Dependent Variable: gi .

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	79.586	2154.255	.000
dt_m	1	53.768	.293	.590
a. Dependent Variable: gi .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.617315	.013300	79.586	46.414	.000	.590844	.643785
dt_m	.001824	.003369	53.768	.542	.590	-.004931	.008579
a. Dependent Variable: gi .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.004264	.000491	8.687	.000	.003403	.005344
Intercept + dt_m [subject = patientid]	UN (1,1)	.011266	.002271	4.962	.000	.007590	.016724
	UN (2,1)	-.000766	.000492	-1.557	.119	-.001731	.000198
	UN (2,2)	.000199	.000180	1.103	.270	3.369288E-5	.001177
a. Dependent Variable: gi .							

Random Effect Covariance Structure (G)[a]

	Intercept | patientid	dt_m | patientid
Intercept | patientid	.011266	-.000766
dt_m | patientid	-.000766	.000199
Unstructured		
a. Dependent Variable: gi .		

Model GI-3 – Full model

Age (centered to the average age of 14 years), brush and sex were added to the initial model (GI-1).

SPSS Syntax

```
MIXED gi BY sexn brush WITH age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=sexn brush age_c sexn*brush sexn*age_c brush*age_c | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	sexn	2		1	
	brush	2		1	
	age_c	1		1	
	sexn * brush	4		1	
	sexn * age_c	2		1	
	brush * age_c	2		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		15		9	

a. Dependent Variable: gi .

Information Criteria[a]	
-2 Log Likelihood	-640.325
Akaike's Information Criterion (AIC)	-622.325
Hurvich and Tsai's Criterion (AICC)	-621.744
Bozdogan's Criterion (CAIC)	-579.410
Schwarz's Bayesian Criterion (BIC)	-588.410
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: gi .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	80.000	2865.429	.000
sexn	1	80	1.435	.235
brush	1	80	.004	.947
age_c	1	80.000	5.056	.027
sexn * brush	1	80.000	.009	.923
sexn * age_c	1	80.000	.061	.806
brush * age_c	1	80.000	.003	.959
a. Dependent Variable: gi .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.604262	.022041	80	27.416	.000	.560399	.648124
[sexn=0]	.029646	.032526	80	.911	.365	-.035084	.094375

[sexn=1]	0[b]	0	.	.	.	.	.
[brush=0]	.003748	.032148	80	.117	.907	-.060229	.067724
[brush=1]	0[b]	0	.	.	.	.	.
age_c	-.019022	.014001	80	-1.359	.178	-.046885	.008841
[sexn=0] * [brush=0]	-.004500	.046236	80.000	-.097	.923	-.096512	.087512
[sexn=0] * [brush=1]	0[b]	0	.	.	.	.	.
[sexn=1] * [brush=0]	0[b]	0	.	.	.	.	.
[sexn=1] * [brush=1]	0[b]	0	.	.	.	.	.
[sexn=0] * age_c	.003850	.015618	80.000	.247	.806	-.027231	.034931
[sexn=1] * age_c	0[b]	0	.	.	.	.	.
[brush=0] * age_c	-.000813	.015624	80.000	-.052	.959	-.031906	.030279
[brush=1] * age_c	0[b]	0	.	.	.	.	.
a. Dependent Variable: gi .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]							
Parameter		Estimate	Std. Error	Wald Z	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Residual		.004658	.000425	10.954	.000	.003895	.005571
Intercept [subject = patientid]	Variance	.008546	.001539	5.553	.000	.006004	.012163
a. Dependent Variable: gi .							

Random Effect Covariance Structure (G)[a]	
	Intercept | patientid
Intercept | patientid	.008546
Identity	
a. Dependent Variable: gi .	

Model GI-4 – Full model, main effects only

SPSS Syntax

```
MIXED gi BY sexn brush WITH age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=sexn brush age_c | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]

		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	sexn	2		1	
	brush	2		1	
	age_c	1		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		7		6	

a. Dependent Variable: gi .

Information Criteria[a]	
-2 Log Likelihood	-640.231
Akaike's Information Criterion (AIC)	-628.231
Hurvich and Tsai's Criterion (AICC)	-627.963
Bozdogan's Criterion (CAIC)	-599.622
Schwarz's Bayesian Criterion (BIC)	-605.622

The information criteria are displayed in smaller-is-better form.
a. Dependent Variable: gi .

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	80	3167.051	.000
sexn	1	80	1.468	.229
brush	1	80	.004	.947
age_c	1	80	5.214	.025
a. Dependent Variable: gi .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.606107	.019102	80.000	31.730	.000	.568093	.644121
[sexn=0]	.027696	.022857	80	1.212	.229	-.017790	.073181
[sexn=1]	0b	0	.	.	.	.	.
[brush=0]	.001491	.022441	80	.066	.947	-.043167	.046150
[brush=1]	0b	0	.	.	.	.	.
age_c	-.017698	.007750	80	-2.283	.025	-.033121	-.002274
a. Dependent Variable: gi .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.004658	.000425	10.954	.000	.003895	.005571
Intercept [subject = patientid]	Variance	.008557	.001541	5.554	.000	.006013	.012179
a. Dependent Variable: gi .							

Random Effect Covariance Structure (G)[a]	
	Intercept | patientid
Intercept | patientid	.008557
Identity	
a. Dependent Variable: gi .	

Model GI-5 – Age

SPSS Syntax

```
MIXED gi WITH age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=age_c | SSTYPE(3)
  /METHOD=ML
/PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimensiona					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	age_c	1		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		3		4	
a. Dependent Variable: gi .					

Information Criteria[a]	
-2 Log Likelihood	-638.761
Akaike's Information Criterion (AIC)	-630.761

Hurvich and Tsai's Criterion (AICC)	-630.634
Bozdogan's Criterion (CAIC)	-611.688
Schwarz's Bayesian Criterion (BIC)	-615.688
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: gi .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	80	3.108.625	.000
age_c	1	80.000	4.301	.041
a. Dependent Variable: gi .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.620594	.011131	80	55.755	.000	.598443	.642745
age_c	-.015391	.007422	80.000	-2.074	.041	-.030160	-.000621
a. Dependent Variable: gi .							

Bootstrap for Estimates of Fixed Effects						
		Bootstrap[a]				
					95% Confidence Interval	
Parameter	Estimate	Bias	Std. Error	Sig. (2-tailed)	Lower	Upper
Intercept	.620594	-5.572621E-6	.004083	.000	.612611	.628593
age_c	-.015391	1.541527E-5	.002659	.000	-.020494	-.010113
a. Unless otherwise noted. bootstrap results are based on 10000 bootstrap samples						

Covariance Parameters

Estimates of Covariance Parameters[a]							
Parameter		Estimate	Std. Error	Wald Z	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Residual		.004658	.000425	10.954	.000	.003895	.005571
Intercept [subject = patientid]	Variance	.008737	.001569	5.568	.000	.006145	.012424
a. Dependent Variable: gi .							

Bootstrap for Estimates of Covariance Parameters							
Parameter		Estimate	Bootstrap[a]				
			Bias	Std. Error	Sig. (2-tailed)	95% Confidence Interval	
						Lower	Upper
Residual		.004658	-.001166	.000387	.001	.002749	.004260
Intercept [subject = patientid]	Variance	.008737	.001138	.000750	.000	.008458	.011436
a. Unless otherwise noted. bootstrap results are based on 10000 bootstrap samples							

Random Effect Covariance Structure (G)[a]	
	Intercept | patientid
Intercept | patientid	.008737
Identity	
a. Dependent Variable: gi .	

Model comparison

Information Criteria	Model GI-1 (unconditional)	Model GI-2 (linear time)	Model GI-3 (full model)	Model GI-4 (main effects)	Model GI-5 (age)
-2 Log Likelihood	-634.572	-637.815	-640.325	-640.231	-638.761
Akaike's Information Criterion (AIC)	-628.572	-625.815	-622.325	-628.231	**-630.761**

Hurvich and Tsai's Criterion (AICC)	-628.496	-625.546	-621.744	-627.963	**-630.634**
Bozdogan's Criterion (CAIC)	**-614.267**	-597.205	-579.410	-599.622	-611.688
Schwarz's Bayesian Criterion (BIC)	**-617.267**	-603.205	-588.410	-605.622	-615.688

The information criteria are displayed in smaller-is-better form.

Bold values indicate the better model.

Model FMPS-1 – Unconditional mean model

SPSS Syntax

```
MIXED fmps
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0,
    ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
  /FIXED=| SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		2		3	
a. Dependent Variable: fmps .					

Information Criteria[a]	
-2 Log Likelihood	-584.302
Akaike's Information Criterion (AIC)	-578.302
Hurvich and Tsai's Criterion (AICC)	-578.226
Bozdogan's Criterion (CAIC)	-563.997
Schwarz's Bayesian Criterion (BIC)	-566.997
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: fmps .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	80	5.747.256	.000
a. Dependent Variable: fmps .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.909475	.011997	80	75.811	.000	.885601	.933349
a. Dependent Variable: fmps .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.005558	.000507	10.954	.000	.004648	.006647
Intercept [subject = patientid]	Variance	.010124	.001825	5.548	.000	.007111	.014414
a. Dependent Variable: fmps .							

Random Effect Covariance Structure (G)[a]	
	Intercept | patientid
Intercept | patientid	.010124
Identity	
a. Dependent Variable: fmps .	

Model FMPS-2–Linear time

SPSS syntax

```
MIXED fmps WITH dt_m
```

```
/CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
  ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
/FIXED=dt_m | SSTYPE(3)
/METHOD=ML
/PRINT=G  SOLUTION TESTCOV
/RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimensiona					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	dt_m	1		1	
Random Effects	Intercept + dt_mb	2	Unstructured	3	patientid
Residual				1	
Total		4		6	
a. Dependent Variable: fmps .					
b. As of version 11.5. the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax. please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-592.339
Akaike's Information Criterion (AIC)	-580.339
Hurvich and Tsai's Criterion (AICC)	-580.070
Bozdogan's Criterion (CAIC)	-551.729
Schwarz's Bayesian Criterion (BIC)	-557.729
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: fmps .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	78.738	3.794.569	.000
dt_m	1	63.993	.635	.428
a. Dependent Variable: fmps .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.904913	.014690	78.738	61.600	.000	.875671	.934154
dt_m	.002795	.003507	63.993	.797	.428	-.004212	.009801
a. Dependent Variable: fmps .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.005229	.000563	9.287	.000	.004234	.006458
Intercept + dt_m [subject = patientid]	UN (1,1)	.013763	.002777	4.957	.000	.009268	.020439
	UN (2,1)	-.001214	.000570	-2.129	.033	-.002331	-9.631640E-5
	UN (2,2)	.000152	.000170	.893	.372	1.687255E-5	.001361
a. Dependent Variable: fmps .							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.013763	-.001214
dt_m | patientid	-.001214	.000152
Unstructured		

a. Dependent Variable: fmps .

Model FMPS-3 – Full model

SPSS Syntax

```
MIXED fmps BY brush sexn WITH dt_m age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
    ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
  /FIXED=brush sexn dt_m age_c brush*sexn brush*dt_m brush*age_c sexn*dt_m sexn*age_c dt_m*age_c |
    SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	brush	2		1	
	sexn	2		1	
	dt_m	1		1	
	age_c	1		1	
	brush * sexn	4		1	
	brush * dt_m	2		1	
	brush * age_c	2		1	
	sexn * dt_m	2		1	
	sexn * age_c	2		1	
	dt_m * age_c	1		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		22		15	

a. Dependent Variable: fmps .
b. As of version 11.5. the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax. please consult the current syntax reference guide for more information.

Information Criteria[a]	
-2 Log Likelihood	-607.131
Akaike's Information Criterion (AIC)	-577.131
Hurvich and Tsai's Criterion (AICC)	-575.552
Bozdogan's Criterion (CAIC)	-505.607
Schwarz's Bayesian Criterion (BIC)	-520.607
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: fmps .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	81.820	4.068.313	.000
brush	1	77.806	.343	.560
sexn	1	78.063	2.884	.093
dt_m	1	70.564	.627	.431
age_c	1	78.355	7.281	.009
brush * sexn	1	81.352	2.158	.146
brush * dt_m	1	64.787	.015	.903
brush * age_c	1	83.260	.178	.674
sexn * dt_m	1	66.332	.070	.792
sexn * age_c	1	83.051	.341	.561

dt_m * age_c	1	62.529	.021	.887
a. Dependent Variable: fmps .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.872787	.026081	86.800	33.464	.000	.820947	.924628
[brush=0]	.016211	.035914	98.612	.451	.653	-.055053	.087475
[brush=1]	0[b]	0	.	.	.	.	.
[sexn=0]	.081007	.036101	97.220	2.244	.027	.009359	.152655
[sexn=1]	0[b]	0	.	.	.	.	.
dt_m	.003350	.005933	57.519	.565	.575	-.008528	.015227
age_c	-.033723	.014885	97.302	-2.266	.026	-.063263	-.004182
[brush=0] * [sexn=0]	-.065187	.044373	81.352	-1.469	.146	-.153469	.023095
[brush=0] * [sexn=1]	0[b]	0	.	.	.	.	.
[brush=1] * [sexn=0]	0[b]	0	.	.	.	.	.
[brush=1] * [sexn=1]	0[b]	0	.	.	.	.	.
[brush=0] * dt_m	.000875	.007181	64.787	.122	.903	-.013466	.015217
[brush=1] * dt_m	0[b]	0	.	.	.	.	.
[brush=0] * age_c	.006372	.015117	83.260	.421	.674	-.023694	.036437
[brush=1] * age_c	0[b]	0	.	.	.	.	.
[sexn=0] * dt_m	-.001933	.007309	66.332	-.265	.792	-.016525	.012658
[sexn=1] * dt_m	0[b]	0	.	.	.	.	.
[sexn=0] * age_c	.008819	.015102	83.051	.584	.561	-.021218	.038857
[sexn=1] * age_c	0[b]	0	.	.	.	.	.
dt_m * age_c	.000360	.002510	62.529	.143	.887	-.004657	.005376
a. Dependent Variable: fmps .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]

Parameter		Estimate	Std. Error	Wald Z	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Residual		.005147	.000546	9.427	.000	.004180	.006336
Intercept + dt_m [subject = patientid]	UN (1,1)	.011640	.002449	4.753	.000	.007707	.017581
	UN (2,1)	-.001145	.000542	-2.111	.035	-.002207	-8.192092E-5
	UN (2,2)	.000179	.000169	1.054	.292	2.782565E-5	.001146
a. Dependent Variable: fmps .							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.011640	-.001145
dt_m | patientid	-.001145	.000179
Unstructured		
a. Dependent Variable: fmps .		

Model FMPS-4 – Main effects

SPSS Syntax

```
MIXED fmps BY brush sexn WITH dt_m age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
    ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
  /FIXED=brush sexn dt_m age_c | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]

		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	brush	2		1	
	sexn	2		1	
	dt_m	1		1	
	age_c	1		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		9		9	
a. Dependent Variable: fmps .					
b. As of version 11.5. the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax. please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-604.285
Akaike's Information Criterion (AIC)	-586.285
Hurvich and Tsai's Criterion (AICC)	-585.705
Bozdogan's Criterion (CAIC)	-543.370
Schwarz's Bayesian Criterion (BIC)	-552.370
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: fmps .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.

Intercept	1	78.700	4.235.977	.000
brush	1	82.109	.350	.556
sexn	1	82.111	3.953	.050
dt_m	1	66.224	.672	.415
age_c	1	81.904	11.383	.001
a. Dependent Variable: fmps .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.890216	.020784	100.425	42.833	.000	.848984	.931448
[brush=0]	-.012961	.021920	82.109	-.591	.556	-.056566	.030644
[brush=1]	0[b]	0	.	.	.	.	.
[sexn=0]	.044381	.022323	82.111	1.988	.050	-2.504178E-5	.088787
[sexn=1]	0[b]	0	.	.	.	.	.
dt_m	.002880	.003513	66.224	.820	.415	-.004133	.009893
age_c	-.025560	.007576	81.904	-3.374	.001	-.040631	-.010489
a. Dependent Variable: fmps .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.005184	.000551	9.407	.000	.004209	.006384
Intercept + dt_m [subject = patientid]	UN (1,1)	.012016	.002500	4.806	.000	.007992	.018066
	UN (2,1)	-.001133	.000540	-2.100	.036	-.002191	-7.547735E-5
	UN (2,2)	.000159	.000167	.949	.343	2.011008E-5	.001252
a. Dependent Variable: fmps .							

Random Effect Covariance Structure (G)[a]

	Intercept | patientid	dt_m | patientid
Intercept | patientid	.012016	-.001133
dt_m | patientid	-.001133	.000159
Unstructured		
a. Dependent Variable: fmps .		

Model FMPS-5 – sex, age

SPSS Syntax

```
MIXED fmps BY brush sexn WITH dt_m age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
    ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
  /FIXED=sexn dt_m age_c | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	sexn	2		1	
	dt_m	1		1	
	age_c	1		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		7		8	
a. Dependent Variable: fmps .					
b. As of version 11.5. the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax. please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-603.937
Akaike's Information Criterion (AIC)	-587.937
Hurvich and Tsai's Criterion (AICC)	-587.474
Bozdogan's Criterion (CAIC)	-549.790
Schwarz's Bayesian Criterion (BIC)	-557.790
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: fmps .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	78.674	4.220.413	.000
sexn	1	82.281	3.840	.053
dt_m	1	66.382	.673	.415
age_c	1	82.244	10.977	.001
a. Dependent Variable: fmps .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.883983	.017950	98.821	49.247	.000	.848366	.919600
[sexn=0]	.043812	.022357	82.281	1.960	.053	-.000662	.088285
[sexn=1]	0[b]	0	.	.	.	.	.
dt_m	.002878	.003509	66.382	.820	.415	-.004127	.009883
age_c	-.024746	.007469	82.244	-3.313	.001	-.039603	-.009888
a. Dependent Variable: fmps .							

b. This parameter is set to zero because it is redundant.

Covariance Parameters

Estimates of Covariance Parameters[a]							
Parameter		Estimate	Std. Error	Wald Z	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Residual		.005186	.000551	9.410	.000	.004211	.006387
Intercept + dt_m [subject = patientid]	UN (1,1)	.012071	.002509	4.811	.000	.008032	.018141
	UN (2,1)	-.001132	.000539	-2.101	.036	-.002188	-7.589830E-5
	UN (2,2)	.000156	.000167	.940	.347	1.942801E-5	.001260
a. Dependent Variable: fmps .							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.012071	-.001132
dt_m | patientid	-.001132	.000156
Unstructured		
a. Dependent Variable: fmps .		

Model FMPS-6 – Age

SPSS Syntax

```
MIXED fmps WITH dt_m age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
    ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
  /FIXED=dt_m age_c | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	dt_m	1		1	
	age_c	1		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		5		7	
a. Dependent Variable: fmps .					
b. As of version 11.5. the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax. please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-600.177
Akaike's Information Criterion (AIC)	-586.177
Hurvich and Tsai's Criterion (AICC)	-585.818
Bozdogan's Criterion (CAIC)	-552.799
Schwarz's Bayesian Criterion (BIC)	-559.799
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: fmps .	

Fixed Effects

Type III Tests of Fixed Effects[a]

Source	Numerator df	Denominator df	F	Sig.
Intercept	1	79.110	4.048.882	.000
dt_m	1	65.537	.523	.472
age_c	1	81.254	8.203	.005
a. Dependent Variable: fmps .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.906141	.014241	79.110	63.631	.000	.877796	.934486
dt_m	.002542	.003515	65.537	.723	.472	-.004476	.009561
age_c	-.021063	.007354	81.254	-2.864	.005	-.035695	-.006431
a. Dependent Variable: fmps .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.005203	.000554	9.385	.000	.004222	.006411
Intercept + dt_m [subject = patientid]	UN (1,1)	.012729	.002606	4.886	.000	.008523	.019012
	UN (2,1)	-.001205	.000555	-2.171	.030	-.002292	-.000117
	UN (2,2)	.000161	.000168	.958	.338	2.073297E-5	.001243
a. Dependent Variable: fmps .							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.012729	-.001205
dt_m | patientid	-.001205	.000161
Unstructured		
a. Dependent Variable: fmps .		

Model comparison

Information Criteria	Model FMPS-1 (unconditional)	Model FMPS-2 (linear time)	Model FMPS-3 (full model)	Model FMPS-4 (main effects)	Model FMPS-5 (sex, age)	Model FMPS-6 (age)
-2 Log Likelihood	-584.302	-592.339	-607.131	-604.285	-603.937	-600.177
Akaike's Information Criterion (AIC)	-578.302	-580.339	-577.131	-586.285	**-587.937**	-586.177
Hurvich and Tsai's Criterion (AICC)	-578.226	-580.070	-575.552	-585.705	**-587.474**	-585.818
Bozdogan's Criterion (CAIC)	-563.997	-551.729	-505.607	-543.370	-549.790	**-552.799**
Schwarz's Bayesian Criterion (BIC)	-566.997	-557.729	-520.607	-552.370	-557.790	**-559.799**

The information criteria are displayed in smaller-is-better form.

Bold values indicate the better model.

Model GIS-1 – Unconditional mean model

SPSS Syntax

```
MIXED gis
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
    ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
  /FIXED=| SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]

		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		2		3	

a. Dependent Variable: gis .

Information Criteria[a]

-2 Log Likelihood	-521.044
Akaike's Information Criterion (AIC)	-515.044
Hurvich and Tsai's Criterion (AICC)	-514.968
Bozdogan's Criterion (CAIC)	-500.739
Schwarz's Bayesian Criterion (BIC)	-503.739

The information criteria are displayed in smaller-is-better form.

a. Dependent Variable: gis .

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	80	4.330.486	.000
a. Dependent Variable: gis .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.912975	.013874	80	65.806	.000	.885366	.940584
a. Dependent Variable: gis .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.006566	.000599	10.954	.000	.005491	.007853
Intercept [subject = patientid]	Variance	.013757	.002439	5.640	.000	.009718	.019474
a. Dependent Variable: gis .							

Random Effect Covariance Structure (G)[a]	
	Intercept | patientid
Intercept | patientid	.013757
Identity	
a. Dependent Variable: gis .	

Model GIS-2 – Linear time

SPSS Syntax

```
MIXED gis WITH dt_m
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
    ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
  /FIXED=dt_m | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT dt_m | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	dt_m	1		1	
Random Effects	Intercept + dt_m[b]	2	Unstructured	3	patientid
Residual				1	
Total		4		6	
a. Dependent Variable: gis .					
b. As of version 11.5. the syntax rules for the RANDOM subcommand have changed. Your command syntax may yield results that differ from those produced by prior versions. If you are using version 11 syntax. please consult the current syntax reference guide for more information.					

Information Criteria[a]	
-2 Log Likelihood	-522.717
Akaike's Information Criterion (AIC)	-510.717
Hurvich and Tsai's Criterion (AICC)	-510.449
Bozdogan's Criterion (CAIC)	-482.107

Schwarz's Bayesian Criterion (BIC)	-488.107
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: gis .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	78.195	3.636.593	.000
dt_m	1	41.194	.017	.897
a. Dependent Variable: gis .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.913634	.015150	78.195	60.304	.000	.883473	.943795
dt_m	-.000543	.004159	41.194	-.131	.897	-.008941	.007855
a. Dependent Variable: gis .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.005843	.000733	7.973	.000	.004570	.007471
Intercept + dt_m [subject = patientid]	UN (1,1)	.014381	.003006	4.785	.000	.009548	.021662
	UN (2,1)	-.000461	.000755	-.610	.542	-.001940	.001019
	UN (2,2)	.000384	.000330	1.165	.244	7.138807E-5	.002067
a. Dependent Variable: gis .							

Random Effect Covariance Structure (G)[a]		
	Intercept | patientid	dt_m | patientid
Intercept | patientid	.014381	-.000461
dt_m | patientid	-.000461	.000384
Unstructured		
a. Dependent Variable: gis .		

Model GIS-3 – Full model

SPSS Syntax

```
MIXED gis BY brush sexn WITH dt_m age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
    ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
  /FIXED=brush sexn dt_m age_c brush*sexn brush*dt_m brush*age_c sexn*dt_m sexn*age_c dt_m*age_c |
    SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	brush	2		1	
	sexn	2		1	
	dt_m	1		1	
	age_c	1		1	
	brush * sexn	4		1	
	brush * dt_m	2		1	
	brush * age_c	2		1	

	sexn * dt_m	2		1	
	sexn * age_c	2		1	
	dt_m * age_c	1		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		21		13	
a. Dependent Variable: gis .					

Information Criteria[a]	
-2 Log Likelihood	-542.237
Akaike's Information Criterion (AIC)	-516.237
Hurvich and Tsai's Criterion (AICC)	-515.048
Bozdogan's Criterion (CAIC)	-454.249
Schwarz's Bayesian Criterion (BIC)	-467.249
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: gis .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	111.591	3.881.194	.000
brush	1	113.950	.270	.604
sexn	1	114.260	3.872	.052
dt_m	1	244.823	.119	.730
age_c	1	113.876	3.545	.062
brush * sexn	1	79.547	.354	.554
brush * dt_m	1	245.035	.042	.839

brush * age_c	1	79.676	.265	.608
sexn * dt_m	1	245.327	2.573	.110
sexn * age_c	1	79.607	3.507	.065
dt_m * age_c	1	246.983	2.853	.092
a. Dependent Variable: gis .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.878451	.027262	104.719	32.222	.000	.824394	.932508
[brush=0]	.001070	.039017	97.612	.027	.978	-.076362	.078503
[brush=1]	0[b]	0	.	.	.	.	.
[sexn=0]	.072833	.039325	96.174	1.852	.067	-.005224	.150889
[sexn=1]	0[b]	0	.	.	.	.	.
dt_m	.003939	.005960	246.713	.661	.509	-.007801	.015678
age_c	-.030760	.016608	89.344	-1.852	.067	-.063757	.002237
[brush=0] * [sexn=0]	-.031674	.053235	79.547	-.595	.554	-.137626	.074277
[brush=0] * [sexn=1]	0[b]	0	.	.	.	.	.
[brush=1] * [sexn=0]	0[b]	0	.	.	.	.	.
[brush=1] * [sexn=1]	0[b]	0	.	.	.	.	.
[brush=0] * dt_m	.001478	.007243	245.035	.204	.839	-.012789	.015744
[brush=1] * dt_m	0[b]	0	.	.	.	.	.
[brush=0] * age_c	-.009257	.017997	79.676	-.514	.608	-.045074	.026560
[brush=1] * age_c	0[b]	0	.	.	.	.	.
[sexn=0] * dt_m	-.011845	.007385	245.327	-1.604	.110	-.026391	.002701
[sexn=1] * dt_m	0[b]	0	.	.	.	.	.
[sexn=0] * age_c	.033680	.017986	79.607	1.873	.065	-.002115	.069476
[sexn=1] * age_c	0[b]	0	.	.	.	.	.
dt_m * age_c	-.004284	.002536	246.983	-1.689	.092	-.009280	.000712
a. Dependent Variable: gis .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]							
Parameter		Estimate	Std. Error	Wald Z	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Residual		.006383	.000583	10.942	.000	.005336	.007635
Intercept [subject = patientid]	Variance	.011270	.002047	5.506	.000	.007895	.016089
a. Dependent Variable: gis .							

Random Effect Covariance Structure (G)[a]	
	Intercept | patientid
Intercept | patientid	.011270
Identity	
a. Dependent Variable: gis .	

Model GIS-4 – Main effects

SPSS Syntax

```
MIXED gis BY brush sexn WITH dt_m age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
    ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
  /FIXED=brush sexn dt_m age_c | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]					
		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	

	brush	2		1	
	sexn	2		1	
	dt_m	1		1	
	age_c	1		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		8		7	
a. Dependent Variable: gis .					

Information Criteria[a]	
-2 Log Likelihood	-529.717
Akaike's Information Criterion (AIC)	-515.717
Hurvich and Tsai's Criterion (AICC)	-515.358
Bozdogan's Criterion (CAIC)	-482.338
Schwarz's Bayesian Criterion (BIC)	-489.338
The information criteria are displayed in smaller-is-better form.	
a. Dependent Variable: gis .	

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	113.247	4.032.361	.000
brush	1	79.969	.214	.645
sexn	1	80.039	2.238	.139
dt_m	1	245.499	.029	.865
age_c	1	79.981	8.554	.004
a. Dependent Variable: gis .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.901014	.023598	91.748	38.181	.000	.854144	.947884
[brush=0]	-.012376	.026764	79.969	-.462	.645	-.065638	.040887
[brush=1]	0[b]	0	.	.	.	.	.
[sexn=0]	.040793	.027266	80.039	1.496	.139	-.013468	.095053
[sexn=1]	0[b]	0	.	.	.	.	.
dt_m	-.000617	.003633	245.499	-.170	.865	-.007772	.006538
age_c	-.027035	.009244	79.981	-2.925	.004	-.045431	-.008639
a. Dependent Variable: gis .							
b. This parameter is set to zero because it is redundant.							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.006565	.000599	10.954	.000	.005489	.007851
Intercept [subject = patientid]	Variance	.012187	.002192	5.560	.000	.008567	.017338
a. Dependent Variable: gis .							

Random Effect Covariance Structure (G)[a]	
	Intercept | patientid
Intercept | patientid	.012187
Identity	
a. Dependent Variable: gis .	

Model GIS-5 – age

SPSS Syntax

```
MIXED gis WITH age_c
  /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001) HCONVERGE(0.
    ABSOLUTE) LCONVERGE(0. ABSOLUTE) PCONVERGE(0.000001. ABSOLUTE)
  /FIXED=age_c | SSTYPE(3)
  /METHOD=ML
  /PRINT=G  SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(patientid) COVTYPE(UN).
```

Mixed Model Analysis

Model Dimension[a]

		Number of Levels	Covariance Structure	Number of Parameters	Subject Variables
Fixed Effects	Intercept	1		1	
	age_c	1		1	
Random Effects	Intercept	1	Identity	1	patientid
Residual				1	
Total		3		4	

a. Dependent Variable: gis .

Information Criteria[a]	
-2 Log Likelihood	-527.320
Akaike's Information Criterion (AIC)	-519.320
Hurvich and Tsai's Criterion (AICC)	-519.193
Bozdogan's Criterion (CAIC)	-500.247
Schwarz's Bayesian Criterion (BIC)	-504.247
The information criteria are displayed in smaller-is-better form.	

a. Dependent Variable: gis .

Fixed Effects

Type III Tests of Fixed Effects[a]				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	80	4.690.262	.000
age_c	1	80	6.529	.013
a. Dependent Variable: gis .				

Estimates of Fixed Effects[a]							
						95% Confidence Interval	
Parameter	Estimate	Std. Error	df	t	Sig.	Lower Bound	Upper Bound
Intercept	.914024	.013346	80	68.485	.000	.887464	.940584
age_c	-.022739	.008899	80	-2.555	.013	-.040449	-.005030
a. Dependent Variable: gis .							

Covariance Parameters

Estimates of Covariance Parameters[a]							
						95% Confidence Interval	
Parameter		Estimate	Std. Error	Wald Z	Sig.	Lower Bound	Upper Bound
Residual		.006566	.000599	10.954	.000	.005491	.007853
Intercept [subject = patientid]	Variance	.012595	.002256	5.583	.000	.008866	.017892
a. Dependent Variable: gis .							

Random Effect Covariance Structure (G)[a]	
	Intercept | patientid
Intercept | patientid	.012595
Identity	
a. Dependent Variable: gis .	

Model comparison

Information Criteria	Model GIS-1 (unconditional)	Model GIS-2 (linear time)	Model GIS-3 (full model)	Model GIS-4 (main effects)	Model GIS-5 (age)
-2 Log Likelihood	-521.044	-522.717	-542.237	-529.717	-527.320
Akaike's Information Criterion (AIC)	-515.044	-510.717	-516.237	-515.717	**-519.320**
Hurvich and Tsai's Criterion (AICC)	-514.968	-510.449	-515.048	-515.358	**-519.193**
Bozdogan's Criterion (CAIC)	**-500.739**	-482.107	-454.249	-482.338	-500.247
Schwarz's Bayesian Criterion (BIC)	-503.739	-488.107	-467.249	-489.338	**-504.247**

The information criteria are displayed in smaller-is-better form.

Bold values indicate the better model.

Raw Data

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s103	E	f	0.224	0.867	0.444	0.833	0	13.40	0
s117	M	m	0.247	0.933	0.481	0.847	0	13.04	0
s131	E	m	0.321	0.900	0.602	1.000	0	16.80	0
s137	E	f	0.290	0.867	0.759	1.000	0	14.26	0
s149	M	f	0.299	1.000	0.542	0.903	0	16.41	0
s151	E	m	0.503	1.000	0.667	1.000	0	14.02	0
s173	E	f	0.231	0.917	0.699	0.972	0	13.45	0
s179	M	f	0.408	1.000	0.773	1.000	0	13.14	0
s183	M	f	0.344	0.950	0.546	0.806	0	14.63	0
s188	E	m	0.426	1.000	0.667	1.000	0	15.06	0
s190	E	m	0.167	0.567	0.500	1.000	0	17.24	0
s193	E	m	0.222	0.867	0.458	0.806	0	15.18	0
s200	M	m	0.160	0.650	0.787	1.000	0	13.76	0
s214	E	f	0.163	0.675	0.389	0.569	0	14.91	0
s219	E	f	0.403	1.000	0.537	1.000	0	14.37	0
s221	E	m	0.242	0.967	0.449	1.000	0	13.46	0
s222	M	m	0.108	0.433	0.532	0.722	0	15.79	0
s226	E	m	0.449	1.000	0.667	1.000	0	15.00	0
s253	M	m	0.494	1.000	0.792	1.000	0	11.46	0
s257	M	f	0.426	1.000	0.694	1.000	0	12.07	0
s269	M	m	0.460	1.000	0.569	1.000	0	15.33	0
s276	M	f	0.353	1.000	0.644	0.931	0	12.05	0
s283	E	m	0.268	1.000	0.792	1.000	0	14.14	0
s309	E	f	0.233	0.933	0.602	0.778	0	15.65	0
s323	E	m	0.307	0.967	0.667	1.000	0	16.13	0
s327	M	m	0.415	1.000	0.750	1.000	0	14.80	0
s358	E	f	0.294	1.000	0.731	1.000	0	12.80	0
s360	M	m	0.346	0.933	0.597	1.000	0	15.53	0
s385	E	f	0.350	0.950	0.764	1.000	0	12.49	0
s413	M	f	0.314	0.950	0.523	1.000	0	13.65	0
s417	E	m	0.279	0.883	0.394	0.319	0	12.64	0

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s429	M	m	0.229	0.950	0.815	1.000	0	15.23	0
s451	M	f	0.346	1.000	0.667	1.000	0	12.46	0
s471	M	f	0.236	0.800	0.542	0.764	0	13.14	0
s472	E	m	0.488	1.000	0.847	1.000	0	13.54	0
s487	M	m	0.217	0.808	0.722	1.000	0	12.71	0
s496	M	m	0.217	1.000	0.551	0.917	0	16.39	0
s501	E	f	0.192	0.867	0.667	1.000	0	12.78	0
s518	M	m	0.376	0.975	0.500	0.944	0	13.65	0
s525	M	f	0.333	1.000	0.741	1.000	0	11.95	0
s532	M	f	0.149	0.633	0.597	0.875	0	13.74	0
s544	M	m	0.289	0.933	0.681	0.917	0	12.98	0
s549	E	f	0.288	0.967	0.667	1.000	0	13.66	0
s550	E	m	0.494	1.000	0.782	1.000	0	12.75	0
s552	M	m	0.176	0.642	0.343	0.556	0	15.51	0
s583	M	f	0.299	0.925	0.514	0.486	0	16.79	0
s598	E	f	0.285	0.900	0.639	0.917	0	16.24	0
s651	M	m	0.351	0.967	0.769	0.931	0	15.47	0
s653	M	m	0.433	1.000	0.486	0.792	0	14.22	0
s655	E	m	0.461	1.000	0.722	1.000	0	15.97	0
s658	M	f	0.174	0.733	0.583	1.000	0	11.59	0
s661	M	m	0.396	1.000	0.667	1.000	0	14.18	0
s673	M	m	0.194	0.817	0.417	0.819	0	11.78	0
s675	M	f	0.369	1.000	0.458	0.556	0	13.10	0
s677	E	f	0.061	0.250	0.412	0.542	0	16.43	0
s692	E	f	0.307	1.000	0.602	1.000	0	13.51	0
s693	E	m	0.225	0.825	0.472	1.000	0	15.15	0
s708	E	f	0.293	0.967	0.778	1.000	0	15.26	0
s710	M	f	0.189	0.783	0.403	0.667	0	15.35	0
s711	M	f	0.296	1.000	0.667	1.000	0	10.65	0
s729	E	m	0.378	0.933	0.667	1.000	0	12.86	0
s740	M	f	0.207	0.717	0.764	1.000	0	13.86	0
s747	E	f	0.458	1.000	0.667	1.000	0	11.17	0
s749	M	m	0.232	0.925	0.384	1.000	0	14.12	0

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s764	E	m	0.379	1.000	0.745	1.000	0	15.83	0
s778	M	f	0.329	0.967	0.676	1.000	0	10.92	0
s790	E	f	0.365	0.883	0.514	0.597	0	12.54	0
s799	E	f	0.439	1.000	0.718	1.000	0	13.99	0
s807	E	m	0.360	0.967	0.611	0.861	0	12.46	0
s810	E	m	0.336	1.000	0.667	0.972	0	15.47	0
s837	E	m	0.326	1.000	0.454	0.847	0	13.88	0
s846	E	f	0.233	0.925	0.838	1.000	0	13.41	0
s857	M	m	0.483	1.000	0.741	1.000	0	12.99	0
s877	M	f	0.415	1.000	0.634	0.833	0	13.74	0
s884	M	m	0.564	1.000	0.750	1.000	0	15.07	0
s911	E	f	0.258	0.825	0.616	1.000	0	15.57	0
s918	E	m	0.333	1.000	0.472	1.000	0	15.81	0
s926	M	f	0.319	0.983	0.759	1.000	0	13.85	0
s938	M	f	0.513	1.000	0.667	1.000	0	13.95	0
s965	E	f	0.253	0.967	0.389	0.806	0	13.36	0
s103	E	f	0.207	0.867	0.361	0.681	28	13.40	1
s117	M	m	0.294	0.975	0.671	1.000	35	13.04	1
s131	E	m	0.354	0.900	0.556	1.000	14	16.80	1
s137	E	f	0.208	0.850	0.745	1.000	28	14.26	1
s149	M	f	0.343	0.950	0.681	1.000	49	16.41	1
s151	E	m	0.429	1.000	0.532	1.000	28	14.02	1
s173	E	f	0.163	0.617	0.630	0.889	20	13.45	1
s179	M	f	0.261	0.958	0.847	1.000	35	13.14	1
s183	M	f	0.176	0.675	0.421	0.653	28	14.63	1
s188	E	m	0.228	0.750	0.556	0.903	41	15.06	1
s190	E	m	0.188	0.733	0.398	0.889	28	17.24	1
s193	E	m	0.249	0.900	0.565	0.903	35	15.18	1
s200	M	m	0.185	0.808	0.644	0.917	21	13.76	1
s214	E	f	0.163	0.683	0.403	0.694	21	14.91	1
s219	E	f	0.256	0.967	0.667	1.000	28	14.37	1
s221	E	m	0.303	1.000	0.579	1.000	28	13.46	1
s222	M	m	0.107	0.383	0.583	0.792	63	15.79	1

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s226	E	m	0.310	1.000	0.597	1.000	56	15.00	1
s253	M	m	0.560	1.000	0.713	1.000	21	11.46	1
s257	M	f	0.379	1.000	0.565	0.722	35	12.07	1
s269	M	m	0.454	1.000	0.667	1.000	28	15.33	1
s276	M	f	0.301	0.967	0.704	1.000	49	12.05	1
s283	E	m	0.203	0.850	0.778	1.000	28	14.14	1
s309	E	f	0.171	0.683	0.435	0.431	21	15.65	1
s323	E	m	0.299	1.000	0.528	0.903	28	16.13	1
s327	M	m	0.393	1.000	0.708	1.000	21	14.80	1
s358	E	f	0.236	0.967	0.634	0.889	28	12.80	1
s360	M	m	0.283	0.900	0.750	1.000	21	15.53	1
s385	E	f	0.353	0.908	0.667	1.000	14	12.49	1
s413	M	f	0.294	0.933	0.546	1.000	34	13.65	1
s417	E	m	0.264	0.950	0.648	0.931	35	12.64	1
s429	M	m	0.276	1.000	0.759	1.000	32	15.23	1
s451	M	f	0.204	0.817	0.481	1.000	26	12.46	1
s471	M	f	0.249	0.867	0.565	0.806	28	13.14	1
s472	E	m	0.188	0.758	0.681	0.917	21	13.54	1
s487	M	m	0.353	1.000	0.829	1.000	27	12.71	1
s496	M	m	0.257	0.917	0.588	1.000	35	16.39	1
s501	E	f	0.165	0.625	0.583	1.000	28	12.78	1
s518	M	m	0.467	1.000	0.667	1.000	21	13.65	1
s525	M	f	0.189	0.750	0.819	1.000	58	11.95	1
s532	M	f	0.133	0.567	0.528	0.958	28	13.74	1
s544	M	m	0.331	0.983	0.657	1.000	28	12.98	1
s549	E	f	0.357	1.000	0.722	1.000	64	13.66	1
s550	E	m	0.483	1.000	0.824	1.000	63	12.75	1
s552	M	m	0.256	0.842	0.384	0.472	28	15.51	1
s583	M	f	0.257	0.783	0.546	0.611	35	16.79	1
s598	E	f	0.338	0.950	0.745	1.000	21	16.24	1
s651	M	m	0.383	0.950	0.759	1.000	21	15.47	1
s653	M	m	0.370	0.925	0.426	0.708	35	14.22	1
s655	E	m	0.539	1.000	0.778	1.000	43	15.97	1

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s658	M	f	0.201	0.850	0.625	1.000	21	11.59	1
s661	M	m	0.332	1.000	0.667	1.000	21	14.18	1
s673	M	m	0.244	1.000	0.421	0.708	71	11.78	1
s675	M	f	0.293	0.983	0.708	0.972	42	13.10	1
s677	E	f	0.111	0.450	0.440	0.583	28	16.43	1
s692	E	f	0.260	0.942	0.565	0.903	28	13.51	1
s693	E	m	0.240	0.933	0.505	1.000	28	15.15	1
s708	E	f	0.268	0.983	0.773	1.000	21	15.26	1
s710	M	f	0.156	0.650	0.417	0.528	28	15.35	1
s711	M	f	0.338	1.000	0.736	1.000	56	10.65	1
s729	E	m	0.324	0.967	0.667	1.000	29	12.86	1
s740	M	f	0.228	0.858	0.611	0.917	35	13.86	1
s747	E	f	0.511	1.000	0.639	0.944	28	11.17	1
s749	M	m	0.239	0.867	0.602	1.000	35	14.12	1
s764	E	m	0.375	1.000	0.722	1.000	28	15.83	1
s778	M	f	0.260	0.900	0.579	1.000	42	10.92	1
s790	E	f	0.299	0.933	0.505	0.778	28	12.54	1
s799	E	f	0.404	1.000	0.718	1.000	64	13.99	1
s807	E	m	0.393	0.967	0.546	0.889	28	12.46	1
s810	E	m	0.188	0.733	0.667	1.000	21	15.47	1
s837	E	m	0.508	1.000	0.528	0.889	28	13.88	1
s846	E	f	0.318	0.975	0.870	1.000	28	13.41	1
s857	M	m	0.319	0.983	0.704	0.917	34	12.99	1
s877	M	f	0.403	1.000	0.657	1.000	71	13.74	1
s884	M	m	0.192	0.750	0.667	1.000	21	15.07	1
s911	E	f	0.263	0.858	0.551	0.958	86	15.57	1
s918	E	m	0.342	1.000	0.588	1.000	21	15.81	1
s926	M	f	0.422	1.000	0.750	1.000	34	13.85	1
s938	M	f	0.479	1.000	0.667	1.000	28	13.95	1
s965	E	f	0.256	0.950	0.500	0.833	28	13.36	1
s103	E	f	0.250	0.942	0.440	0.694	91	13.40	2
s117	M	m	0.318	1.000	0.662	1.000	77	13.04	2
s131	E	m	0.375	1.000	0.606	1.000	27	16.80	2

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s137	E	f	0.211	0.900	0.815	1.000	51	14.26	2
s149	M	f	0.279	0.933	0.486	0.750	112	16.41	2
s151	E	m	0.463	1.000	0.542	1.000	49	14.02	2
s173	E	f	0.158	0.650	0.519	0.972	97	13.45	2
s179	M	f	0.285	1.000	0.917	1.000	63	13.14	2
s183	M	f	0.317	1.000	0.486	0.889	49	14.63	2
s188	E	m	0.201	0.750	0.528	0.861	69	15.06	2
s190	E	m	0.204	0.833	0.454	0.736	50	17.24	2
s193	E	m	0.193	0.775	0.495	0.819	56	15.18	2
s200	M	m	0.178	0.750	0.556	0.722	77	13.76	2
s214	E	f	0.181	0.725	0.375	0.667	42	14.91	2
s219	E	f	0.293	0.933	0.667	1.000	56	14.37	2
s221	E	m	0.329	1.000	0.560	1.000	56	13.46	2
s222	M	m	0.135	0.567	0.583	0.597	91	15.79	2
s226	E	m	0.419	1.000	0.681	1.000	86	15.00	2
s253	M	m	0.324	0.983	0.667	1.000	42	11.46	2
s257	M	f	0.286	1.000	0.667	0.972	56	12.07	2
s269	M	m	0.379	1.000	0.588	0.903	49	15.33	2
s276	M	f	0.286	1.000	0.819	1.000	77	12.05	2
s283	E	m	0.239	0.967	0.667	1.000	56	14.14	2
s309	E	f	0.207	0.842	0.417	0.347	37	15.65	2
s323	E	m	0.293	0.950	0.537	0.792	49	16.13	2
s327	M	m	0.407	1.000	0.722	1.000	51	14.80	2
s358	E	f	0.232	0.850	0.611	1.000	98	12.80	2
s360	M	m	0.297	0.950	0.713	1.000	49	15.53	2
s385	E	f	0.360	1.000	0.667	1.000	42	12.49	2
s413	M	f	0.286	0.950	0.509	0.847	101	13.65	2
s417	E	m	0.251	1.000	0.616	0.792	70	12.64	2
s429	M	m	0.361	1.000	0.634	1.000	56	15.23	2
s451	M	f	0.218	0.917	0.472	1.000	47	12.46	2
s471	M	f	0.318	0.867	0.667	1.000	56	13.14	2
s472	E	m	0.224	0.925	0.676	1.000	77	13.54	2
s487	M	m	0.308	1.000	0.903	1.000	56	12.71	2

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s496	M	m	0.311	0.967	0.625	0.944	63	16.39	2
s501	E	f	0.208	0.733	0.681	1.000	91	12.78	2
s518	M	m	0.403	1.000	0.574	1.000	51	13.65	2
s525	M	f	0.203	0.842	0.773	1.000	98	11.95	2
s532	M	f	0.181	0.758	0.528	0.931	70	13.74	2
s544	M	m	0.238	0.758	0.653	1.000	49	12.98	2
s549	E	f	0.364	1.000	0.727	1.000	99	13.66	2
s550	E	m	0.292	0.933	0.787	1.000	84	12.75	2
s552	M	m	0.151	0.600	0.472	0.472	70	15.51	2
s583	M	f	0.292	0.942	0.718	0.917	63	16.79	2
s598	E	f	0.349	0.950	0.667	1.000	63	16.24	2
s651	M	m	0.344	0.942	0.681	0.972	42	15.47	2
s653	M	m	0.243	0.767	0.644	0.735	63	14.22	2
s655	E	m	0.503	1.000	0.801	1.000	77	15.97	2
s658	M	f	0.267	0.933	0.523	1.000	43	11.59	2
s661	M	m	0.283	0.967	0.593	0.833	45	14.18	2
s673	M	m	0.233	0.933	0.449	0.764	99	11.78	2
s675	M	f	0.246	0.900	0.671	0.917	56	13.10	2
s677	E	f	0.100	0.417	0.435	0.569	49	16.43	2
s692	E	f	0.267	0.975	0.588	0.972	56	13.51	2
s693	E	m	0.238	0.900	0.514	0.847	63	15.15	2
s708	E	f	0.301	0.967	0.694	0.917	77	15.26	2
s710	M	f	0.233	0.850	0.569	0.861	56	15.35	2
s711	M	f	0.336	1.000	0.676	1.000	91	10.65	2
s729	E	m	0.386	0.925	0.542	0.806	61	12.86	2
s740	M	f	0.325	0.883	0.606	0.903	71	13.86	2
s747	E	f	0.340	0.900	0.523	0.944	57	11.17	2
s749	M	m	0.251	0.900	0.597	0.903	63	14.12	2
s764	E	m	0.372	1.000	0.708	1.000	54	15.83	2
s778	M	f	0.274	0.950	0.500	1.000	70	10.92	2
s790	E	f	0.203	0.833	0.458	0.542	49	12.54	2
s799	E	f	0.343	1.000	0.667	1.000	99	13.99	2
s807	E	m	0.294	1.000	0.727	1.000	70	12.46	2

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s810	E	m	0.274	0.950	0.667	1.000	84	15.47	2
s837	E	m	0.442	1.000	0.588	0.833	56	13.88	2
s846	E	f	0.263	0.942	0.884	1.000	63	13.41	2
s857	M	m	0.290	0.900	0.741	0.917	55	12.99	2
s877	M	f	0.265	0.950	0.667	1.000	84	13.74	2
s884	M	m	0.228	0.883	0.616	0.931	49	15.07	2
s911	E	f	0.261	0.958	0.523	1.000	105	15.57	2
s918	E	m	0.379	0.983	0.620	1.000	54	15.81	2
s926	M	f	0.354	1.000	0.644	1.000	84	13.85	2
s938	M	f	0.488	1.000	0.667	1.000	48	13.95	2
s965	E	f	0.243	1.000	0.528	0.833	49	13.36	2
s103	E	f	0.256	0.967	0.472	0.708	119	13.40	3
s117	M	m	0.314	1.000	0.523	1.000	108	13.04	3
s131	E	m	0.408	1.000	0.634	1.000	64	16.80	3
s137	E	f	0.246	0.908	0.667	1.000	77	14.26	3
s149	M	f	0.375	0.950	0.528	1.000	161	16.41	3
s151	E	m	0.518	1.000	0.667	0.986	77	14.02	3
s173	E	f	0.240	0.900	0.694	1.000	125	13.45	3
s179	M	f	0.293	1.000	0.755	1.000	91	13.14	3
s183	M	f	0.225	0.883	0.449	0.778	70	14.63	3
s188	E	m	0.367	1.000	0.713	1.000	103	15.06	3
s190	E	m	0.197	0.808	0.421	0.583	77	17.24	3
s193	E	m	0.279	0.975	0.477	0.736	77	15.18	3
s200	M	m	0.167	0.742	0.667	1.000	105	13.76	3
s214	E	f	0.246	0.850	0.417	0.569	73	14.91	3
s219	E	f	0.274	0.967	0.667	1.000	91	14.37	3
s221	E	m	0.201	0.817	0.537	1.000	84	13.46	3
s222	M	m	0.151	0.617	0.514	0.694	119	15.79	3
s226	E	m	0.249	0.892	0.667	1.000	105	15.00	3
s253	M	m	0.399	1.000	0.667	1.000	63	11.46	3
s257	M	f	0.311	0.967	0.685	0.986	77	12.07	3
s269	M	m	0.394	1.000	0.551	0.903	70	15.33	3
s276	M	f	0.469	1.000	0.722	1.000	119	12.05	3

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s283	E	m	0.214	0.925	0.611	0.889	105	14.14	3
s309	E	f	0.138	0.533	0.431	0.403	98	15.65	3
s323	E	m	0.274	1.000	0.560	0.819	78	16.13	3
s327	M	m	0.418	1.000	0.708	1.000	106	14.80	3
s358	E	f	0.249	0.825	0.611	0.958	133	12.80	3
s360	M	m	0.371	1.000	0.676	1.000	90	15.53	3
s385	E	f	0.342	0.950	0.667	1.000	63	12.49	3
s413	M	f	0.289	0.933	0.556	0.889	140	13.65	3
s417	E	m	0.233	0.950	0.644	0.764	84	12.64	3
s429	M	m	0.350	1.000	0.588	0.903	85	15.23	3
s451	M	f	0.203	0.850	0.486	0.806	78	12.46	3
s471	M	f	0.286	0.950	0.667	1.000	84	13.14	3
s472	E	m	0.253	1.000	1.000	1.000	119	13.54	3
s487	M	m	0.300	1.000	0.829	1.000	77	12.71	3
s496	M	m	0.276	0.950	0.597	0.875	84	16.39	3
s501	E	f	0.225	0.842	0.528	1.000	112	12.78	3
s518	M	m	0.224	0.950	0.634	1.000	105	13.65	3
s525	M	f	0.250	0.900	0.681	1.000	140	11.95	3
s532	M	f	0.346	1.000	0.667	1.000	105	13.74	3
s544	M	m	0.222	0.858	0.713	1.000	84	12.98	3
s549	E	f	0.285	0.983	0.667	1.000	134	13.66	3
s550	E	m	0.315	1.000	0.829	1.000	112	12.75	3
s552	M	m	0.267	0.900	0.431	0.361	91	15.51	3
s583	M	f	0.194	0.700	0.491	0.528	91	16.79	3
s598	E	f	0.194	0.825	0.667	1.000	95	16.24	3
s651	M	m	0.263	0.775	0.671	1.000	91	15.47	3
s653	M	m	0.274	0.950	0.662	0.958	91	14.22	3
s655	E	m	0.338	1.000	0.704	1.000	98	15.97	3
s658	M	f	0.258	0.933	0.565	0.889	91	11.59	3
s661	M	m	0.271	0.983	0.639	0.917	76	14.18	3
s673	M	m	0.239	0.933	0.468	0.694	120	11.78	3
s675	M	f	0.289	0.983	0.667	1.000	85	13.10	3
s677	E	f	0.106	0.442	0.421	0.569	77	16.43	3

patientid	brush	sex	pim	fmps	gi	gis	dt	age	visit
s692	E	f	0.317	1.000	0.514	0.833	91	13.51	3
s693	E	m	0.249	0.967	0.486	0.778	98	15.15	3
s708	E	f	0.364	1.000	0.810	1.000	95	15.26	3
s710	M	f	0.196	0.758	0.458	0.722	77	15.35	3
s711	M	f	0.367	1.000	0.556	1.000	112	10.65	3
s729	E	m	0.343	0.967	0.620	1.000	92	12.86	3
s740	M	f	0.157	0.658	0.639	1.000	112	13.86	3
s747	E	f	0.332	1.000	0.509	1.000	77	11.17	3
s749	M	m	0.235	0.883	0.597	0.833	110	14.12	3
s764	E	m	0.486	1.000	0.769	1.000	72	15.83	3
s778	M	f	0.381	1.000	0.806	1.000	98	10.92	3
s790	E	f	0.285	0.967	0.528	0.958	77	12.54	3
s799	E	f	0.311	1.000	0.667	1.000	134	13.99	3
s807	E	m	0.368	0.983	0.741	1.000	91	12.46	3
s810	E	m	0.194	0.733	0.681	1.000	126	15.47	3
s837	E	m	0.451	1.000	0.611	0.917	77	13.88	3
s846	E	f	0.219	0.900	0.810	1.000	105	13.41	3
s857	M	m	0.318	1.000	0.782	1.000	97	12.99	3
s877	M	f	0.317	0.900	0.569	1.000	91	13.74	3
s884	M	m	0.263	0.917	0.606	0.889	70	15.07	3
s911	E	f	0.365	0.967	0.583	1.000	140	15.57	3
s918	E	m	0.317	0.933	0.667	1.000	79	15.81	3
s926	M	f	0.329	1.000	0.569	1.000	105	13.85	3
s938	M	f	0.499	1.000	0.741	1.000	98	13.95	3
s965	E	f	0.550	1.000	0.597	0.861	91	13.36	3

Appendices

APPENDIX 1: SAMPLE CONSENT FORM (for parents/guardians)

CONSENT FORM FOR PARTICIPATION IN CLINICAL TRIALS

(for parents/guardians)

SCHOOL OF DENTISTRY,
NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS

Study number:

Title: Comparison of electric 3D and manual toothbrushes in patients with fixed orthodontic appliances.

School/Department : Department of Orthodontics, University of Athens

Researchers: Marili Mylonopoulou

Eudoxie Pepelassi

Phoebus Madianos

Demetrios J. Halazonetis

You are requested to participate in a research program that is supported by the University of Athens. The following information is provided to you in order to decide if you wish to participate in this study.

Aim

The aim of this study is to investigate which brush is more effective on cleaning your teeth when wearing braces, an electric or a manual one?

Procedures

Eighty people of both sexes, between 12-16 years old will take place in this study. They should have:

- ✓ Good general health according to a recent full medical history

- ✓ Fixed labial orthodontic appliances (metallic brackets), on all teeth from central incisor to first molar, in both the maxillary and the mandibular arch, placed at least two months before the patient is accepted into the study and no more than two years. Patient should have fixed appliances for three more months after evaluation. Molars should be banded.
- ✓ No extractions of permanent teeth planned in their orthodontic treatment.

You will be asked to stay in this study for about three months. During this period you will have to visit the dental school about 3-4 times and the examination will be done before your appointment with your orthodontist, with average visit duration of half an hour. Sometimes it may be necessary to visit the dental school even if you do not have an appointment with your orthodontist.

All patients will get oral hygiene instructions in the Orthodontic Clinic of the University of Athens by a trained dentist.

Patients will be randomly assigned in two groups. Half of the patients will get the electric toothbrush and the other half a manual toothbrush, according to the group to which they will be assigned. Then you will have to brush with the brush that will be given to you for three months.

Patient monthly visits

Visits will be planned at intervals of 4 weeks, in line with the scheduled orthodontic visits.

Visit 1 (4 weeks)

Measurements, filling the questionnaire and discussion of problems

Visit 2 (8 weeks)

Measurements, filling the questionnaire and discussion of problems if needed

Visit 3 (12 weeks)

Measurements, filling the questionnaire and discussion of problems if needed, interview with the participant, give brushes to patient as a gift, instructions for electric toothbrush, if not already given.

If you do not use the brush given or do not follow the instructions given you will be asked to inform us via a questionnaire given in every visit. In addition you will be asked not to inform the researchers, except for one, which brush you use.

Once you enter the study, you will be asked not to use other toothbrushes and toothpastes except the ones given to you. You will also be asked not to floss or use interdental brushes, not to use whitening or fluoride products, to inform us if you visit your dentist for treatment, including cleaning, periodontal treatment or topical fluoridation and not to take part in other trials.

Exclusion criteria

You can't take part in this study if you:

- ✓ Have active caries
- ✓ Have periodontitis
- ✓ Have tooth agenesis (excluding third molars)
- ✓ Currently use an electric toothbrush
- ✓ Syndromes and craniofacial deformities
- ✓ More than two cervical and/or proximal fillings
- ✓ Dental prosthesis or dental implants
- ✓ Smoke
- ✓ Took antibiotics during the last 2 months
- ✓ Take medication that may result in gingival enlargement (anticonvulsants, immunosuppressants, and calcium channel blockers)
- ✓ Have peri-oral or intra-oral piercing
- ✓ Have cardiac or other medical problems that requires antibiotic prophylaxis for dental treatment
- ✓ Participate in other trials

Possible dangers and problems

No significant harms are expected to occur related to this study. The brushes and toothpastes given are safe and used in everyday life by millions of people. All measurements will be performed by a trained dentist.

Anticipated adverse events will be handled at the DentUoA without cost to the patients.

Cost

You don't have to pay any money in order to participate in this study.

Electric and manual toothbrushes and toothpastes for all participants will be provided by Oral-B. Miscellaneous costs will be covered by the participating departments.

Benefits

If you take part in this study, you will monthly check ups of your oral hygiene for free. The cost of the treatment you receive from the Department of the Graduate Program of Orthodontics will not change. In case you need any other dental treatment in the meanwhile (e.g. prosthetics, endodontics, occlusion) you will have to pay for it.

At the end of the study all brushes will be given to you as a gift (one electric and one manual).

Participation in this study will not affect your lifestyle. In any case cleaning and frequent monitoring will improve your oral health.

Payment

You will not get any money in order to participate in this study.

In the end of the study all brushes will be given to you as a gift (one electric and one manual).

Findings

You will be informed for any new findings that come out during our research and may affect your decision to continue participating in our study.

Confidentiality

Complete confidentiality will be detained for all files but there is no guarantee that such information can not be disclosed in court or other legal process. However, even in that case, your name will not be mentioned in any publication or reference.

Right to non-participation or withdrawal

You can withdraw from this study whenever you wish. Your withdrawal will not affect your ability to receive or continue your treatment at the Dental School of Athens, or other privileges that you may have, nor will your refusal to participate in the program affect your ability to receive or continue your treatment at the Dental School of Athens or get other benefits you have. However, if you withdraw from the study before it is over you will not take the brushes as a gift.The investigator of this research has the right to terminate your participation at any time. This may be due to your non-expected response or non- successful completion of the instructions given to you, or because the study has entirely stopped.

Guarantee that all your questions will be answered

If you have additional questions about this study, please contact the Principal Investigator Mylonopoulou Ioulia-Maria at 6970206531.

This program has been reviewed and approved by the Ethics Committee of the Dental School of the University of Athens. If there are any questions related to the Commission, please contact the Department Chair at (telephone number) via Mrs……

I have read all the information above and agree to participate in this study. I would like to receive a copy of the consent form when it is signed.

_____ _____

Signature of parent/guardian Date

_____ _____

Signature of responsible researcher Date

APPENDIX 2: SAMPLE ASSENT FORM (for patients 12-16 years old)

ASSENT FORM FOR PARTICIPATION IN CLINICAL TRIALS

(for patients 12-16 years old)

SCHOOL OF DENTISTRY
NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS

Study number:

Title: Comparison of electric 3D and manual toothbrushes in patients with fixed orthodontic appliances.

School/Departement : Departement of Orthodontics, University of Athens

Researchers: Marili Mylonopoulou

Eudoxie Pepelassi

Phoebus Madianos

Demetrios J. Halazonetis

The doctors mentioned above will conduct a clinical trial.

Before your participation in the survey would like to know that:

You do not have to participate in this study if you do not want to.

You can leave the study whenever you want to.

If you decide to interrupt, there will be no problems regarding your doctors.

Sometimes there are great benefits for people involved in such studies, but in some cases benefits do not arise. You will be informed in more detail about it.

We would like you to know the reason why you have been asked to participate in this research.

What this aim of this study?

The aim of this study is to investigate which brush is more effective on cleaning your teeth when wearing braces, an electric or a manual one?

What is going to happen during this study:

Eighty people of both sexes, between 12-16 years old will take place in this study. They should have:

- ✓ Good general health according to a recent full medical history
- ✓ Fixed labial orthodontic appliances (metallic brackets), on all teeth from central incisor to first molar, in both the maxillary and the mandibular arch, placed at least two months before the patient is accepted into the study and no more than two years. Molars should be banded.
- ✓ No extractions of permanent teeth planned in their orthodontic treatment.

You will be asked to stay in this study for about three months. During this period you will have to visit the dental school about 3-4 times and the examination will be done before your appointment with your orthodontist, with average visit duration of half an hour. Sometimes it may be necessary to visit the dental school even if you do not have an appointment with your orthodontist.

You will get oral hygiene instructions at the beginning of the study in the Orthodontic Clinic of the University of Athens by a trained dentist.

Patients will be randomly assigned in two groups. Half of the patients will get the electric toothbrush and the other half a manual toothbrush, according to the group to which they will be assigned. Then you will have to brush with the brush that will be given to you for six months.

If you do not use the brush given or do not follow the instructions given you will be asked to inform us via a questionnaire given in every visit. In addition you will be asked not to inform the researchers, except for one, which brush you use.

Once you enter the study, you will be asked not to use other toothbrushes and toothpastes except the ones given to you. You will also be asked not to floss or use interdental brushes, not to use whitening or fluoride products, to inform us if you visit your dentist for treatment,

including cleaning, periodontal treatment or topical fluoridation and not to take part in other trials.

Is this study going to cause any harm to me?

No significant harms are expected to occur during this study. The brushes and toothpastes given are safe and used in everyday life by millions of people. The tooth cleaning will be performed by a trained dentist.

What are the benefits for me?

If you take part in this study, you will get monthly check-ups of your oral hygiene for free. In the end of the study all brushes will be given to you as a gift (one electric and one manual).

Participation in this study will not affect your lifestyle. In any case, cleaning and frequent monitoring will improve your oral health.

Will I get any money for participating?

You will not get any money in order to participate in this study.

Who can I contact for additional questions?

If you have additional questions about this study, please contact the Principal Investigator Mylonopoulou Ioulia-Maria at 6970206531.

If you sign below, you give your consent for participation in this study.

_____ _____

Signature of participant Date

_____ _____

Signature of responsible researcher Date

APPENDIX 3: SAMPLE CLINICAL PERIODONTAL TISSUES ASSESSMENT FORM

Clinical Periodontal Tissues Assessment Form

Secondary Assessment Form

Subject Initials_____Subject Number_____Date_____

Circle the time period for this evaluation:

Baseline	1 Month	2 Months	3 Months End of study

Modified Silness and Löe Plaque index (PI-M): (buccal)

15	14	13	12	11	21	22	23	24	25

45	44	43	42	41	31	32	33	34	35

Modified Full mouth plaque score (FMPS-M): (buccal)

15	14	13	12	11	21	22	23	24	25

45	44	43	42	41	31	32	33	34	35

Modified Gingival index (GI-M): (buccal)

16	15	14	13	12	11	21	22	23	24	25	26

46	45	44	43	42	41	31	32	33	34	35	36

Modified Simplified Gingival index (GI-SM): (buccal)

16	15	14	13	12	11	21	22	23	24	25	26

46	45	44	43	42	41	31	32	33	34	35	36