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CARACTERÍSTICAS DA HIGIENE BUCAL ASSOCIADAS À ABRASÃO GENGIVAL E AO RISCO DE PROGRESSÃO PARA RECESSÃO GENGIVAL

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Tese apresentado ao Curso de Doutorado do Programa de Pós Graduação em Ciências Odontológicas, Área de Concentração em Odontologia, ênfase em Periodontia, da Universidade Federal de Santa Maria (UFSM, RS), como requisito parcial para obtenção do grau de **Doutor em Ciências Odontológicas.**

Orientador: Prof. Dr. Fabricio Batistin Zanatta

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RESUMO

CARACTERÍSTICAS DA HIGIENE BUCAL ASSOCIADAS À ABRASÃO GENGIVAL E AO RISCO DE PROGRESSÃO PARA RECESSÃO GENGIVAL

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A abrasão gengival (AG) é definida como uma perda de substância ou da estrutura da gengiva e/ou da mucosa oral causada por forças mecânicas e/ou químicas. Hipotetiza-se que AGs sobrepostas, causadas pela escovação dental diária, pode levar ao início e/ou progressão da recessão gengival (RG). Assim, a presente tese é composta por dois artigos, cujo desfechos principais são AG e RG. O primeiro estudo, de delineamento observacional transveral, objetivou verificar associações entre características da higiene bucal e AG em 688 indivíduos residentes em uma área rural do sul do Brasil. A extensão da AG foi determinada pelo número de abrasões, por indivíduo. As associações entre AG e variáveis de nível sítio, dente e indivíduo foram determinadas por meio da regressão de Poisson multinível. Frequência de escovação $\geq 2x$ ao dia (RR=2,03; IC 95%: 1,12 – 3,00), escovação com escova de cerdas duras/médias (RR=2,32; IC 95%: 1,29 - 3,45), biofilme dental visível (RR=0,87; IC 95%: 0,79 – 0,99) e inflamação gengival (RR=0,80; IC 95%: 0,62 - 0,95) foram significativamente associadas com a extensão de AG. O segundo estudo foi uma metanálise em rede (NMA), cujo objetivo foi identificar qual (ais) característica/desenho das escovas dentais oferecem menor risco de ocorrência de AG e RG. As bases de dados MEDLINE (PubMed), EMBASE, Cochrane (CENTRAL), Scopus Web of Science e Lilacs foram pesquisadas por ensaios clínicos randomizados (ECRs), que tenham comparado dois ou mais tipos de escovas dentais quanto aos desfechos de AG e RG. No total, seis e sete ECRs foram elegíveis para AG e RG, respectivamente, comparando quatro tipos de intervenções para cada desfecho [(escovas manuais com 1)cerdas arredondadas, 2)cerdas pontiagudas, 3)cerdas em diferentes alturas) e 4) escovas elétricas]. Não foram encontradas diferenças significativas entre os quatro grupos, para ambos os desfechos. A análise da superfície abaixo da curva de ranqueamento cumulativo posicionou as escovas manuais com filamentos arredondados e filamentos em diferentes alturas em primeiro lugar e segundo lugares, respectivamente para o desfecho RG. Para AG, nas mesmas posições ficaram as escovas elétricas e as escovas manuais com filamentos arredondados, respectivamente. Ainda, os resultados das metanálises diretas mostraram que escovas de cerdas macias são protetoras para AG quando comparadas às de cerdas médias [0,73 (IC 0,58;0,91)] e, que escovas elétricas apresentam menor progressão de RG quando comparadas às escovas manuais [-0,11 (CI -0,17; -0,04)]. Esses resultados suportam a hipótese que, dentre as diferentes opções de escovas dentais macias, as diferenças de desenho/característica não parecem exercer um efeito importante na AG e RG, sugerindo que outros fatores (ex. técnica/força de escovação, biotipo gengival) tenham um papel preponderante no desenvolvimento de ambos desfechos.

Palavras-chave: Recessão gengival. Abrasão gengival. Transversal. Metanálise

ABSTRACT

CHARACTERISTICS OF ORAL HYGIENE ASSOCIATED WITH GINGIVAL ABRASION AND THE RISK OF PROGRESSION TO GINGIVAL RECESSION

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Gingival abrasion (GA) is defined as a loss of substance or structure of the gingiva and/or oral mucosa caused by mechanical and/or chemical forces. It is hypothesized that overlapping AGs, caused by daily tooth brushing, can lead to the onset and/or progression of gingival recession (GR). Thus, the present thesis is composed of two articles, whose main outcomes are GA and GR. The first study, with a cross-sectional observational design, aimed to verify associations between oral hygiene characteristics and GA in 688 individuals living in a rural area in southern Brazil. The extent of GA was determined by the number of abrasions per individual. The associations between GA and variables at the site, tooth and individual level were determined using multilevel Poisson regression. Brushing frequency ≥ 2 times a day (RR=2.03; 95% CI: 1.12 – 3.00), brushing with a hard/medium bristle brush (RR=2.32; 95% CI: 1.29 - 3.45), visible dental biofilm (RR=0.87; 95% CI: 0.79 - 0.99) and gingival inflammation (RR=0.80; 95% CI: 0.62 - 0.95) were significantly associated with the extension of GA. The second study was a network meta-analysis (NMA), whose objective was to identify which feature(s)/design of toothbrushes offer the lowest risk of occurrence of AG and GR. The MEDLINE (PubMed), EMBASE, Cochrane (CENTRAL), Scopus Web of Science and Lilacs databases were searched for randomized controlled trials (RCTs) that have compared two or more types of toothbrushes for GA and GR outcomes. In total, six and seven RCTs were eligible for GA and RG, respectively, comparing four types of interventions for each outcome [(manual toothbrushes with 1) rounded bristles, 2) tapered bristles, 3) bristles at different heights) and 4) power toothbrushes]. No significant differences were found between the four groups for both outcomes. Analysis of the surface under the cumulative ranking curve placed hand brushes with rounded filaments and filaments at different heights in first and second place, respectively, for the GR outcome. For GA, power toothbrushe and manual brushes with rounded filaments were in the same positions, respectively. Also, the results of direct meta-analyses showed that soft bristle brushes are protective for GA when compared to medium bristles [0.73 (CI 0.58;0.91)] and that power toothbrushe present less GR progression when compared to manual brushes [-0.11 (CI -0.17; -0.04)]. These results support the among the different soft toothbrush options, that, design/characteristics do not seem to exert an important effect on GA and GR, suggesting that other factors (eg brushing technique/force, gingival biotype) play a major role in the development of both outcomes.

Keywords: Gingival recession. Gingival abrasion. Cross-sectional. Meta-analysis

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1 INTRODUÇÃO

Na prevenção e tratamento de doenças bucais, a higiene bucal adequada é de primordial valor. (DANSER et al., 1998) Quando usada de forma eficiente, a escovação dentária pode prevenir cáries e doenças periodontais e melhorar a saúde bucal dos indivíduos (CLAYDON, 2008). No entanto, o simples ato de limpar os dentes pode causar traumas nos tecidos orais moles e duros (HENNEQUIN et al., 2011).

As deformidades mucogengivais, em especial as recessões gengivais (RG), são um grupo de condições que ocorrem com frequência em adultos com altos e baixos padrões de higiene bucal. (CORTELINE et al., 2018). Sua prevalência >3mm é apresentada entre 22,4 (ALBANDAR et al.,1994) e 75,4% (RIOS et al., 2014) em amostras representativas de populações urbanas. Por outro lado, nas populações rurais, poucos estudos são encontrados e a prevalência se apresenta entre 55,6% em indígenas (RONDEROS et al., 2001) e 94,7% em população idosa na índia (BHARATEESH; KOKILA, 2014). Embora a etiologia das recessões gengivais permaneça incerta, pode-se considerar sua relação a múltiplos fatores predisponentes (KASSAB; COHEN, 2003; CORTELLINI, 2018). Dentre estes fatores, a escovação dentária de forma inadequada, o fenótipo gengival e a direção vestibular do movimento ortodôntico são considerados os mais importantes (CORTELLINI et al., 2018; HEASMANet al., 2017).

Hipotetiza-se que lesões epiteliais, que se apresentam de forma superficial ou com exposição do tecido conjuntivo chamadas de abrasões gengivais (AG) (VERSTEEG et al., 2005), quando sobrepostas pelo trauma da escovação diária, poderiam levar ao início e/ou progressão da RG (JOSHIPURA,1994; ADDY E HUNTER 2003). Na literatura, diversos fatores tem sido relacionados às AG, comoo acabamento das cerdas/filamentos (VERSTEEG et al., 2005,; 2008), a força de escovação (BREITENMOSER; MORMANN; MUHLEMANN, 1979; DANSER et al., 1998; VAN DER WEIJDEN, et al., 2004), o tipo de cerdas (CARVALHO et al., 2007; NIEMI; SANDHOLM; AINAMO, 1984), a forma de empunhadura das escovas dentais (NIEMI; AINAMO; ETEMADZADEH, 1987), a escovação com e sem dentifrício (CAPOROSSI et al., 2016; NIEMI; SANDHOLM; AINAMO, 1984; VERSTEEG et al., 2005) e a frequência de escovação (SANGNES; GJERMO, 1976).

Com relação a escovas elétricas comparadas a escovas manuais, evidências de curto e longo prazo observaram o desenvolvimento de AG após a escovação (BAAB; JOHNSON, 1989; WALSH et al., 1989, JOHNSON; MCINNES, 1994, TEREZHALMY et al., 1994, VAN DER WEIJDEN et al., 1994, HEASMAN et al. 1999). Apesar da maioria

deles ter encontrado associação entre uso de escovas dentais de cerdas duras com AG , há muitas controvérsias entre os achados, justificadas possivelmente pela heterogeneidade metodológica dos estudos. Considerando o desenvolvimento ou a progressão de RG, a revisão sistemática de Rajapakse et al., (2007) apontou fatores associados a escovação dentária comumente aceitos como fatores de risco às recessões gengivais. Porém, há carência de evidências que demonstrem claramente o mecanismo de desenvolvimento da lesão., .

Pode-se esperar que as abrasões gengivais superficiais cicatrizem naturalmente, mas não está claro quais hábitos de higiene levam a maior número de AG e qual perfil/característica da escova dental pode afetar aumentar o risco de RG. Dada a possibilidade de uma relação entre características da escovação e da morfologia da escova de dente com abrasão gengival e recessão gengival; e considerando a necessidade de evidências epidemiológicas em com alta prevalência de RG (AHN 2011; WHANG 2007), o objetivo da presente Tese foi avaliar a associação entre hábitos diários de higiene bucal e AG em uma amostra populacional representativa de indivíduos residentes em uma área rural do sul do Brasil, e comparar, através de uma Metanálise em rede (NMA), o efeito de diferentes características/designs de escovas dentais no desenvolvimento de AG e RG. Para isso, dois estudos científicos foram conduzidos, os quais seguem na sequência da Tese.

2. ARTIGO 1:

Associação entre características de higiene bucal e abrasão gengival em uma população rural do sul do Brasil - Análise multinível

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Association between oral hygiene characteristics and gingival abrasion in a rural population in southern Brazil - Multilevel analysis

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Running title: Oral hygiene and gingival abrasion in a rural population

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Abstract

Aim: The aim of the present cross-sectional study was to evaluate associations between

gingival abrasion (GA) and oral hygiene characteristics in individuals living in a rural area of

southern Brazil.

Materials and Methods: A representative population-based sample of individuals living in a

rural area in southern Brazil over 15 years of age with more than 5 teeth was investigated. The

extent of GA was determined based on the total number of abrasions per individual. The

strength of associations between GA and site-level, tooth-level, and individual-level variables

was determined using adjusted multilevel Poisson regression analysis with a conceptual

hierarchical approach to calculate rate ratios (RR).

Results: 595 individuals dentate aged 15 to 82 years were analyzed for associations. In the

adjusted models, brushing frequency > twice a day (RR=2.03; 95% CI: 1.12 - 3.00) and

brushing with a hard/medium-bristle toothbrush (RR=2.32; 95% CI: 1.29 - 3.45) were

significantly associated with more extensive GA. In contrast, subjects with a higher index of

visible plaque (RR=0.87; 95% CI: 0.79 – 0.99) and gingival inflammation (RR=0.80; 95%

CI: 0.62 - 0.95) showed lower AG.

Conclusions: The extent of GA was independently associated with greater brushing

frequency and the use of a toothbrush with harder bristles in residents of a rural area.

KEY WORDS: Gingival abrasion; rural health; oral hygiene; cross-sectional study.

Clinical Relevance

Scientific rationale for study: It is well established that GR is associated with oral hygiene

characteristics. However, the association between AG and oral hygiene characteristics that

can cause GR has not been previously reported.

Principal findings: GA was independently associated with the gingival recession, dentin

hypersensitivity, greater brushing frequency, and harder bristles. In contrast, subjects with a

higher index of visible plaque and gingival inflammation showed lower AG.

Practical implications: Our findings confirm the multifactorial associated factors of GA,

underscoring the importance of the management of certain daily hygiene habits for the

possible reduction in GA and consequently the formation of GR.

Introduction

Mucogingival deformities, such as gingival recession (GR), are a group of conditions that are frequently found in adults regardless of oral hygiene practices (Serino et al., 1994; Loe et al., 1992; Corteline et al., 2018). GR (> 3 mm) is estimated to affect 22.4% (Albandar & Kingman, 1994) to 75.4% (Rios et al., 2014) of individuals in representative samples of urban populations. The few studies conducted with rural populations report rates of 55.6% and 94.7% in an indigenous population (Ronderos et al., 2001) and among older people in India (Bharateesh & Kokila, 2014), respectively.

Although the etiology of GR remains uncertain, associations with multiple predisposing factors have been considered (Kassab & Cohen, 2003; Cortellini et al., 2018). Traumatic tooth brushing has been implicated as a contributing factor for decades (Khocht, 1993; Kassab & Cohen, 2003; Heasman et al., 2017). It is hypothesized that gingival abrasion (GA) (Versteeg et al., 2005) caused by the trauma of daily brushing can lead to the onset and/or progression of GR (Joshipura, 1994; Addy and Hunter, 2003).

GA is a reversible, localized, epithelial injury. It may be a superficial lesion of the keratinized epithelial layer, a puncture wound, or mechanical erosion of the epithelium, which may extend into the submucosa and expose the connective tissue (Versteeg et al., 2005). The terms soft tissue or gingival abrasion, damage, injury, laceration, lesion, recession, and ulceration are used interchangeably (Hennequin-Hoenderdos et al., 2016). The visualization of such lesions is facilitated by dyes applied to the soft tissues, such as toluene blue or erythrosine (Breitenmoser et al., 1979; Niemi et al., 1986; Niemi, 1987; Addy & Hunter, 2003).

The association between brushing trauma and GR has been evaluated in several studies (Rajapakse et al., 2007; Heasman et al., 2015; Ranzan et al., 2019). However, there is a lack of research evaluating GA as a possible causal factor of GR. Regarding factors associated with GA, Carvalho et al. (2007) and Ranzan et al. (2019) found a twofold greater risk of GA when using hard bristle compared to soft bristle toothbrushes. However, it seems that the type of toothbrush filament (tapered or end-rounded) is not critical for GA (Hoogteijling et al., 2017). Moreover, no studies have addressed associations between the development of GA and other toothbrushing variables, such as brushing time and frequency, amount and type of toothpaste, and time between changing toothbrushes.

The aim of the present study was to evaluate associations between daily oral hygiene habits and gingival abrasion in a representative population-based sample of individuals residing in a rural area in southern Brazil. Our hypothesis is that a greater brushing frequency and the use of brushes with stiffer bristles are associated with a greater extent of GA.

Materials and Methods

Study design

The present cross-sectional study was part of a larger epidemiological survey, whose target population was individuals ≥ 15 years of age residing in rural areas of the municipality of Rosário do Sul, State of Rio Grande do Sul, Brazil. Fieldwork was carried out between March 2015 and May 2016.

Ethical considerations

This study received approval from the Human Research Ethics Committee of the Federal University of Santa Maria (certificate number: 37862414.5.0000.5346) and was conducted in accordance with the standards of the regional research ethics committee and the Declaration of Helsinki. Each participant received a full explanation of the study objectives and procedures and agreed to participate by signing a statement of informed consent. Individuals less than 18 years of age needed the authorization of a legal guardian through a signature on a specific statement of informed consent.

Sample

The representative sample of individuals aged 15 years or older residing in the rural area of Rosário do Sul was obtained using the multistage probability sampling method. Thirty rural census tracts were evaluated, from the 6 districts of Rosário do Sul, which were divided into three strata (small, medium and large), according to the number of households. Three random sequences were generated in the Research Randomizer program and allowed all six districts to be evaluated. All subjects aged 15 years and older were considered eligible for the study sample. Exclusion criteria were presence of systemic disease/condition that contraindicates clinical examination or requirement a prophylactic regimen of antibiotics

before it, diagnosis/ family report of psychiatric or mental problems, and alcohol or drug intoxication. The sample size of the main survey was calculated considering the worst-case scenario of periodontitis (hypothetical prevalence of 50%) adjusted for a finite population. Assuming a 4% level of precision, design effect of 1.3, and confidence interval of 95%, the minimum sample size was estimated to be 580 individuals. This value was increased by 15% (667 individuals) to compensate for the non-response rate. A total of 1087 individuals were considered eligible, 397 (36.5%) of whom did not participate in the survey. In total, 688 individuals were included (Ferreira et al., 2018). For the present secondary analysis, 71 edentulous and 22 with less than five teeth were excluded, leading to 595 individuals (89.7%).

The post-hoc statistical power of the analyzed sample was estimated by taking into account the following parameters: 1) unpaired design; 2) α error of 0.05; 3) differences in mean and standard deviation (SD) of overall GA scores between exposed and unexposed groups for brushing frequency (< twice daily: 4.87 [SD: 3.03] and \geq twice daily: 7.02 [SD: 5.95]) and brush type (extra soft/soft: 3.61 [SD: 3.12] and medium/hard: 6.82 [SD: 6.07]). Taking these parameters into account, the power of the sample was 96% for brushing frequency and 94% for brush type.

Training and calibration

The examiners underwent training to perform the clinical evaluations both before and during the study. Training involved definitions of clinical measures and correct measuring techniques. Reproducibility was determined using replicated periodontal measures at ≥ 1000 sites to ensure calibration for the periodontal examination. Intra-class correlation coefficients (ICCs) before the study ranged from 0.92 to 0.96 for probing pocket depth (PPD) and 0.91 to 0.93 for clinical attachment level (CAL). Training and calibration exercises were conducted a second time during the study, when ICCs ranged from 0.88 to 0.90 for PPD and 0.88 to 0.89 for CAL. Thus, reproducibility was considered satisfactory (ICC > 0.80). The research team also tested the data collection procedures in a pilot study (Ferreira et al., 2018).

Theoretical training was conducted for gingival abrasion, with information on how to perform the measurements and the measurement sites. Clinical training when then conducted on patients with an experienced periodontist demonstrating how to perform gingival staining and how to assess areas of GA. Lastly, calibration was performed with two independent evaluators using photographs of two-tone gingival staining (two-tone disclosing solution, Young Dental Manufacturing, Missouri, USA).

Interview and clinical examination

Two trained dentists (SCD and JB) performed the interviews individually with each participant to collect data on demographic/socioeconomic characteristics, smoking status, oral habits, and dental visits. Clinical examinations were conducted in a mobile unit equipped with a complete dental office, artificial light, and other basic amenities by two trained, calibrated examiners (JB and MC). All permanent fully erupted teeth, excluding third molars, were examined with a manual periodontal probe (six sites per tooth: mesiobuccal, mid-buccal, distobuccal, distolingual, mid-lingual and mesiolingual). The following parameters were achieved: visible plaque, marginal gingival bleeding (Ainamo & Bay, 1975), probing pocket depth (PPD), bleeding on probing (BoP), clinical attachment loss (CAL). Were examined with a periodontal probe (UNC-15 probe, Neumar®, São Paulo, Brazil). Periapical radiographs were also performed (Ferreira et al. 2019; Ortigara et al. 2021).

Independent variables

The independent variables were sex (female/male), self-reported skin color (white/non-white), age in years (terciles: ≤ 39/40-54/≥ 55), income (> Brazilian monthly minimum wage [BMMW]/≤ the BMMW, which was R\$750.00 [equivalent to approximately US\$250 during the study period]), schooling (≤ eight/> eight full years of study [corresponding to an elementary school education in Brazil]), smoking (non-smoker [never smoked]/former smoker/current smoker], toothbrushing frequency (≥ twice per day/< twice per day), type of toothbrush bristles (extra-soft to soft/medium to hard), proximal hygiene (yes [uses]/no [does not use]), frequency of dental visits (≥ once per year/< once per year), use of toothpaste (use/non-use), amount of toothpaste used (small to reasonable/medium to large amount), and self-reported hypersensitivity (yes or no). Gingival recession was calculated by subtracting clinical attachment loss (CAL) from pocket probing depth (PPD). The visible plaque index (Ainamo & Bay, 1975) and gingival bleeding index (Ainamo & Bay, 1975) were evaluated dichotomously at each site evaluated. Periodontitis was defined as stages 1/2 or stages 3/4 (Caton et al., 2018).

Dependent variable

Gingival abrasion (a surrogate variable of gingival recession) on soft tissues was evaluated and recorded for all teeth, except third molars, using the method described by Danser et al. (1998). The gums were stained with Mira-2-Tone solution (Young Dental

Manufacturing, Missouri, USA) for better visualization of areas where the surface of the oral epithelium was peeling (gingival abrasion). A variable amount (four to six drops) of the solution was spread over the gums with cotton rolls. A periodontal probe (UNC-15 probe, Neumar®, São Paulo, Brazil) placed on the long axis of the injury was used to measure the size of the abrasions. The largest diameter of an abrasion determined its size. Abrasions were rated as small (≤ 5 mm) or large (> 5 mm) and the total number was recorded. The gingival tissues were divided into three areas: cervical (cervical free gingiva), interdental (papillary free gingiva), and mid-gingival (adhered gingiva), as shown in Fig. 1.

Data analysis

Initially, we conducted descriptive statistics incorporating the weights originated from the sampling design using the "SVY" command for complex samples of the STATA program and presented the data according to the presence of GA. GA was categorized according to its extent as a count variable, in which abrasions in the buccal sites of all teeth (interdental, cervical, and mid-gingival areas) were summed and the total number of GA was considered for each individual.

Progressive selection was used in the multilevel Poisson regression models to test associations between GA and distal, intermediate, and proximal determinants using a theoretical hierarchical structure (Figure 3): site level, tooth level, and individual level, respectively. The individual level was divided into the following blocks: Block 1 – demographic and socioeconomic variables; Block 2 – behavioral and systemic variables; Block 3 – oral health variables; and Block 4 – oral hygiene variables (Victora, Huttly, Fuchs, & Olinto, 1997). Variables for the multilevel analysis were included based on theoretical reasons/criteria and not only on the statistical model. Block 1 was used to adjust Block 2 and the result was used to adjust the subsequent block until obtaining the final model. In the final model, associations were determined after adjustments for variables on the same or higher level that remained in the multivariate model. This strategy enabled the estimation of rate ratios and respective 95% confidence intervals (CIs) adjusted for the effects. Data analysis was performed using the STATA 14 software (Stata Corporation, College Station, TX, USA).

Results

A total of 1092 patients were initially eligible for examination. Five individuals were excluded and 399 declined to participate in the study. The response rate was 63% (688/1087). The reasons for non-participation are presented in the study flowchart (Figure 1). 688 individuals were clinically examined, among which 595 were dentate, with more than five teeth present. Thus, the final sample was composed of 595 individuals aged between 15 and 82 years.

The majority of the sample was white (68.3%), earned more than the monthly minimum wage (71.2%), and had \leq eight years of schooling (72.1%). Almost half were former smokers or current smokers (47.6%). Regarding hygiene habits, 94.5% of the individuals brushed their teeth \geq twice/day, 86.8% used some device for proximal hygiene, 50% used a soft bristle toothbrush, and 50% used a medium/hard bristle brush (Table 1).

A total of 33.8% of younger individuals (≤ 39 years) and 60.3% of those with an income > the monthly minimum wage had more extensive GA (cervical, interdental, and midgingival areas) compared to the oldest age group and individuals who earned less than the monthly minimum wage. About 80% of individuals who brushed their teeth more than twice a day and 55% of those who used a small or reasonable amount of toothpaste had GA. Individuals who used a medium/hard bristle toothbrush had more GA in the cervical region compared to the other areas. Individuals with reported hypersensitivity had more GA in the mid-gingival region compared to the other areas (Table 1).

Table 2 displays the results of the unadjusted and adjusted multilevel Poisson regression analyses. In both models, females, individuals with GR, those with hypersensitivity, those who brushed more than twice a day, and those who used a medium/hard bristle toothbrush had more extensive GA. Females had an average of 23% (RR = 1.23; 95% CI: 1.03 to 1.48) more extensive GA compared to males. Individuals with GR had 6.37-fold (95% CI: 4.02 – 9.19) more extensive GA compared to those without GR. Individuals who brushed > twice a day had 2.03-fold (95% CI: 1.12 – 3.00) more extensive GA than those who brushed < twice a day. Individuals who used a hard/medium-bristle toothbrush had 2.32-fold (CI 95%: 1.29 - 3.45) more extensive GA compared to those who used a soft bristle brush. In contrast, subjects with a higher index of visible plaque (RR=0.87; 95% CI: 0.79 – 0.99) and gingival inflammation (RR=0.80; 95% CI: 0.62 – 0.95) showed lower AG. The extent of GA was 13% (RR = 0.87; 95% CI: 0.79 – 0.99) lower in individuals with more plaque compared to those with less plaque and 20% (RR = 0.80; 95% CI: 0.62 – 0.95) lower in those with gingival bleeding compared to those without gingival bleeding.

Discussion -ARRUMAR

The present findings support the hypothesis that brushing one's teeth more than twice per day and using a toothbrush with medium/hard bristles increase the extent of GA twofold in individuals residing in rural areas in southern Brazil. Additionally, more extensive GA was found in individuals with GR and those who reported having hypersensitivity. In contrast, subjects with a higher index of visible plaque and gingival inflammation showed lower AG.To the best of our knowledge, this is the first study to assess GA as a primary outcome measure and associate it with oral hygiene habits adopting a multilevel strategy. Therefore, this study contributes new information to the field.

GR has been associated with worse esthetic problems, increased susceptibility to root caries, dental hypersensitivity (Smith, 1997; Kssab and Cohen, 2003; Daprile et al. 2007; Gatto et al., 2007), and a poorer quality of life (Wagner et al., 2016), demonstrating the major concern of this condition in periodontal epidemiology. The main etiological factor of GR is the progression of periodontitis (Corteline et al., 2018). Epidemiological data on the association between GA and GR are scarce. The present findings revealed that individuals with GR had an average of 6.37-fold (95% CI: 4.02 – 9.19) more extensive GA compared to their counterparts. Moreover, higher scores of visible plaque and gingival inflammation at the site-level presented with lower AG extensions, demonstrating the greater risk of GA among individuals with better oral hygiene. The adjusted multilevel model was controlled for periodontitis. Thus, GA can act as an independent co-factor in the progression of GR even in individuals with periodontitis.

Dentin hypersensitivity exerts a negative impact on quality of life due to the discomfort caused by external stimuli. This condition has been widely studied and is related to GR (Douglas-de-Oliveira et al. 2018). The association between brushing trauma and GR was confirmed in previous studies (Rajapakse et al., 2007; Heasman et al., 2015; Ranzan et al., 2019). Our data showed an independent association between dentin hypersensitivity and GA, with a twofold increase in the mean rate of GA in individuals who reported having hypersensitivity. Taking GA as a proxy for brushing force, this information suggests a reduction in brushing force for the management of hypersensitivity complaints.

Previous cross-sectional studies showed that the most frequent brushing factors associated with GR are brushing frequency (Paloheimo et al., 1987; Vehkalahti, 1989; Khocht et al., 1993; Checchi et al., 1999; Tezel et al., 2001; Daprile et al., 2007; Chrysanthakopoulos, 2011; Chrysanthakopoulos, 2013), bristle hardness (Khocht et al., 1993; Chrysanthakopoulos,

2011) and brushing time (Tezel et al., 2001). Indeed, brushing twice a day or more led to a twofold increase in the extent of GA in the present investigation. The same twofold increase was found when medium/hard bristles were used, which is in agreement with data reported in previous studies (Breitenmoser et al., 1979; Danser et al., 1998; Niemi et al., 1998; Niemi et al., 1984; Sandholm et al., 1982; Van der Weijden and Hioe, 2005). Carvalho et al. (2007) and Ranzan et al. (2019) also found that the risk of tissue damage was twice as high with hard brushes compared to soft brushes. Zanatta et al. (2011) conducted a randomized double-blind split-mouth clinical trial comparing the use of brushes with soft and medium bristles and found an increase in the prevalence of GA in the cervical region after the use of a medium toothbrush.

This study has limitations that should be addressed. GA is a dynamic condition and may only reflect the last brushing performed. For the data collection, the participants were previously scheduled for the examination. Thus, they may have performed traumatic brushing in an attempt to brush "better" prior to the clinical examination. However, this Hawthorne effect is difficult to control and is virtually implicit in studies with clinical data collection. Another limitation is that we did not collect data on the gingival biotype due to the difficulties in measuring this variable. Regarding the GA assessment, the subjects were not asked if they were bothered by the AG, unlike the hypersensitivity to which it was recorded based on the patient's report. Therefore, it is considered a limitation. Moreover, in terms of the design, cross-sectional observations for GA yield only information on associations for hypotheses to be made (Rios et al. 2014) and are insufficient for understanding how the GR appear and increase. Longitudinal studies should be performed to determine what the risk indicators are and how AG can increase and cause GR in different populations.

The present study confirms that certain daily oral hygiene habits are associated with GA. These results can contribute to the establishment of prevention strategies focused on reducing important outcomes that exert a negative impact on oral health-related quality of life, such as gingival recession and dentin hypersensitivity. Studies involving the investigation of oral health conditions in residents of rural areas are necessary due to the limited access of this population to medical and dental care. Thus, the problems and needs of this population can be identified to enable the planning of health policies aimed at universality and equity, which are factors that affect oral health and have consequences for quality of life.

Conclusion

The present findings indicate that gingival abrasion is independently associated with dentin hypersensitivity, gingival recession, a greater brushing frequency and toothbrush bristle hardness. In contrast, subjects with a higher index of visible plaque and gingival inflammation showed lower AG.

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Table 1. Characteristics of study sample according to cervical, interdental and mid-gingival abrasion (GA)

N (%) Variable

	Total	GA Cervical	GA Interdental	GA Mid-gingival	Full presence of GA
Sex	292(49.9%)	72(48.0%)	99(53.8%)	77(46.6%)	248(42.3%)
Female	293(50%)	78(52.0%)	85 (46.2%)	88(53.3%)	251(42.9%)
Male Skin color White	400(68.3%)	103(68.6%)	131(71.2%)	111(67.2%)	345(58.9%)
Non-white	185(31.6%)	47(31.3%)	53(28.8%)	54(32.7%)	154(26.3%)
Age* ≤ 39 years 40-54 years ≥ 55 years	213(36.4%) 211(36.0%) 193(32.9%)	62(41.3%) 48(32.0%) 40(26.6%)	79(42.9%) 65(35.3%) 40(21.7%)	57(34.5%) 56(33.9%) 52(31.5%)	198 33.8%) 169(28.8%) 132(22.5%)
Income (BMWM)† >1.0 (>750) ≤1.0 (≤750)	416(71.1%) 165(28.2%)	107(71.33%) 43(28.67%)	127(70.1%) 54(29.8%)	119(73.1%) 44(26.9%)	353(60.3%) 141(24.1%)
Schooling (years) >8 years ≤8 years	144(24.6%) 422(72.1%)	43(28.6%) 107(71.3%)	52(28.4%) 131(71.5%)	44(26.67%) 121(73.3%)	139 (23.7%) 359(61.3%)
Smoking Non-smoker Former/current smoker	306(52.3%) 279(47.6.8%)	124(83.2%) 25(16.7%)	156(85.2%) 27(14.7%)	141(85.9%) 23(14.0%)	421(71.9%) 75(58.5%)
Brushign frequency ≥ twice/Day	553(94.5%)	143(95.3%)	174(95%)	155(93.9%)	472(80.6%)
< twice/Day	33(5.6%)	7(4.6%)	9(5.9%)	10(6.0%)	26(4.4%)
Dental visit ≥ 1x/year < 1x/year	266(45.4%) 320(17.0%)	69(46.0%) 81(54.0%)	97(52.7%) 87(47.2%)	71(43.2%) 93(56.7%)	237(40.5%) 261(44.6%)
Toothbrush type	320(17.0%)	81(34.0%)	87(47.270)	93(30.7%)	201(44.0%)
Extra soft/soft Medium/Hard	272(46.4%) 313(53.5%)	79 (48%) 85(51.8%)	92(48%) 99(52%)	77(44.6%) 98(56%)	248(46.7%) 282(53.2%)
Proximal hygiene					
Yes No	508(86.8%) 77(13.1%)	130 (87.2%) 19(12.7%)	157(86%) 26(14.2%)	146(89%) 19(11.5%)	433(74.0%) 418(71.4%)
Hypersensitivity					
Yes	247(42.2%)	78(56.9%)	78 (46.4%)	87(57.2%)	243(41.5%)
No	288(49.2%)	59(43%)	90 (53.5%)	65(42.7%)	214(36.5%)
Dentifrice (quantity)					
Small/reasonable	316(54.3%)	77(52%)	99(54.3%)	92(55%)	268(55%)
Medium/large	265(45.6%)	71(47.9%)	83(45.6%)	73(44.2%)	227(45.8%)

^{*} Tercile †BMMW: Brazilian monthly minimum wage approximately US\$250 during study period.

Table 2: Association between extent of GA and variables on the site, tooth and individual levels.

1.00 0.89 (0.70 – 0.98) 1.00 0.74 (0.41 – 0.96) Tooth-level variables 1.00 6.14 (3.35 – 8.92) dividual-level variables tic and socioeconomic va 1.00 1.18 (1.02 – 1.33) 1.00 0.86 (0.59 – 1.14)	1.00 1.23 (1.03 – 1.48) 1.00
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1.00 0.74 (0.41 – 0.96) Tooth-level variables 1.00 6.14 (3.35 – 8.92) dividual-level variables ic and socioeconomic variables 1.00 1.18 (1.02 – 1.33)	0.87 (0.79 - 0.99) 1.00 $0.80 (0.62 - 0.95)$ 1.00 $6.37 (4.02 - 9.19)$ ariables 1.00 $1.23 (1.03 - 1.48)$ 1.00
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1.00	1.00
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0.92 (0.63 – 1.20)	0.83 (0.31 - 1.24) 1.02 (0.79 - 1.25)
0.92 (0.03 - 1.20)	1.02(0.79 - 1.23)
1.00	1.00
	1.07 (0.81 – 1.34)
(3.1.	,
1.00	1.00
. ,	0.95 (0.70 - 1.23)
Behavioral variables	
1.00	1.00
	1.00
1.18 (0.88 - 1.40)	1.04(0.72-1.36)
1.00	1.00
	0.96 (0.73 – 1.19)
	3.53 (3.73 1.15)
1.00	1.00
0.89 (0.69 - 1.08)	0.93 (0.70 - 1.15)
	1.00
2.02(1.56 - 2.61)	2.06(1.49-2.55)
0.05 (0.96 1.07)	0.04 (0.92.1.02)
	0.94 (0.82-1.03)
	0.98 (0.74 – 1.29) Behavioral variables 1.00 1.18 (0.88 – 1.46) 1.00 0.90 (0.66 – 1.25) Oral Health variables

Brushing frequency		
< twice/day	1.00	1.00
≥ twice/day	1.84 (1.05 - 2.61)	2.03(1.12 - 3.00)
Brush type		
Extra soft/soft	1.00	1.00
Medium/hard	2.19 (1.37 – 3.01)	2.32(1.29 - 3.45)
Dentifrice (quantity)		
Small/reasonable	1.00	1.00
Medium/large	1.14(0.79-1.72)	1.08(0.77-1.59)
· •		

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BMMW: Brazilian monthly minimum wage % US\$250 during study period.
Unadjusted* and adjusted ** Multilevel logistic regression

Figure 1. Division of tooth-related soft tissues into three areas for assessment of gingival abrasions: cervical, interdental, and mid-gingival (modified method described by DANSER et al., 1998).

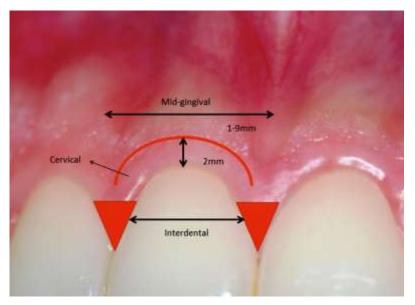


Figure 2. Study flowchart

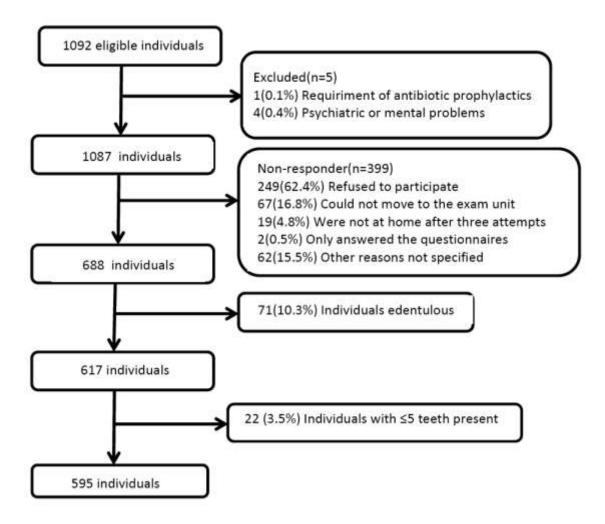
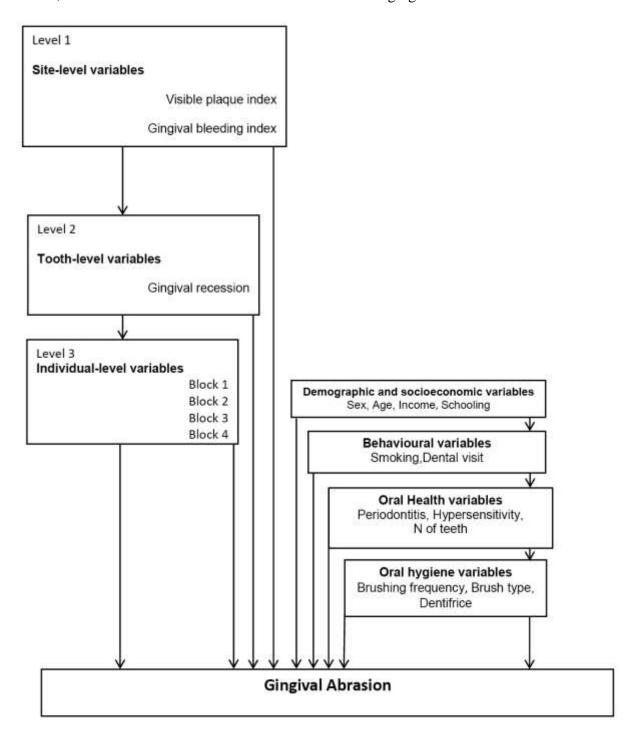


Figure 3. Conceptual hierarchical structure of association between demographic, socioeconomic, and behavioral variables related to oral health and gingival abrasion



3. ARTIGO 2:

O tipo e a morfologia das escovas dentais são importantes para a abrasão gengival e prevenção da recessão gengival? Uma Revisão Sistemática e Meta-análises de Rede

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Are the type and morphology of toothbrushes important for gingival abrasion and gingival recession prevention? A Systematic Review and Network Meta-analyses

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Running title: Toothbrushes and development of gingival abrasion and recession

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Abstract

Aim: The aim of this systematic review and network meta-analyses (NMA) was to identify the best characteristic of toothbrush (e.g. types and morphologies) capable to prevent or reduce the occurrence of gingival abrasion (GA) and gingival recession (GR).

Materials and Methods: The MEDLINE (PubMed), EMBASE, Cochrane (CENTRAL), Scopus, and Web of Science databases were searched for randomized clinical trials (RCTs) comparing two or more types of toothbrushes (e.g. bristle/filament morphologies) regarding GA and/or GR. The quality of evidence was rated according to the RoB 2.0 Cochrane's tool and certainty of evidence by GRADE's tool extension for NMA. For both outcomes, mean differences were used to carry out a Bayesian hierarchical framework to compare multiple treatments.

Results: Six and seven RCTs were eligible in NMA for GA and GR, respectively, comprising four different treatments for each outcome. No significant differences were detected between the characteristics of the toothbrushes for both outcomes. In direct comparisons, soft bristles were a protective factor for GA when compared to medium bristle toothbrushes [0.73 (CI 0.58;0.91)] and powered toothbrushes minimized the occurrence of GR when compared to the manual ones [-0.11 (CI -0.17; -0.04)]. SUCRA ranked toothbrushes with end-rounded bristles first.

Conclusions: Manual toothbrushes with end-rounded bristles and powered toothbrush showed less GR occurrence than the other groups evaluated. Manual toothbrushes with soft bristles are safe for GA. However, a cautious interpretation is necessary due to the low number of direct comparison arms.

KEYWORDS: Gingival abrasion, Gingival recession, Oral hygiene, Toothbrush, Systematic review

Clinical Relevance

Scientific rationale for the study: It is not clear which characteristics of daily toothbrushing are associated with the risk of GA and GR to provide safe recommendations in clinical practice

Principal findings: Manual toothbrushes with end-rounded soft bristles and powered toothbrush cause lower rates of GA and GR, respectively.

Practical implications: End-rounded soft manual toothbrushes and powered toothbrush are safe for GA and GR, respectively. However, among the different options of manual soft toothbrushes, the different characteristics seem to have little difference in effects over GA and GR.

Introduction

Gingival abrasion (GA) is defined as a loss of substance or structure of the gingiva and/or oral mucosa caused by mechanical and chemical forces, especially by vigorous toothbrushing (Breitenmoser, 1979; Versteeg et al., 2005). Clinically, GA is characterized as a clear sign of rupture, ulceration, or erosion of the outer surface of the gingiva (Sandholm, Niemi, and Ainamo 1982). It is hypothesized that superimposed GA caused by daily toothbrushing associated with lack of keratinized tissue may lead to the onset and/or progression of gingival recession (GR) (Cortellini et al. 2018), although this hypothesis is not yet supported by clear scientific evidence (Rajapakse et al., 2007; Addy and Hunter 2003, Rosema et al. 2008).

GR is a group of conditions that occur frequently in adults, regardless of oral hygiene standards (Serino et al., 1994; Loe et al., 1992, Cortellini et al., 2018), defined as the displacement of the gingival margin apically to the enamel-cemental junction (Cortellini et al., 2018). The prevalence of GR ≥1 mm in epidemiological studies ranges from 57.9% (Albandar e Kingman et al, 1999) to 99.7% (Rios et al., 2014) for urban populations, and 47.8% to 85% in individuals with high standard of oral hygiene (Checchi, Daprile, Gatto, & Pelliccioni, 1999; Matas, Sentis, & Mendieta, 2011). The presence of GR may bring many negative effects, such as functional (Bharateesh & Kokila, 2014; Costa et al., 2014; Dhaliwal, Palwankar, Khinda, & Sodhi, 2012; Kularatne & Ekanayake, 2007) and aesthetic problems (Smith, 1997; Kassab and Cohen, 2003).

It has been postulated that GA is more associated with toothbrush characteristics than dentifrice components (Sagnes 1976; Breitenmoser et al. 1979). Studies that evaluated different modalities of powered toothbrushes (Van der Weijden et al. 2011) and toothbrush filaments (Hoogteijling et al. 2017) found no evidence of an oral hygiene device characteristic that was more associated with the risk of GA and/or GR. On the other hand, there are recommendations regarding the characteristics of the oral hygiene habits and devices that would be associated with a lower risk of GA and, thereafter, the establishment and progression of GR (e.g., bristle hardness, type of filament, brushing technique and amount of dentifrice), based on clinical practice and expert opinions (ADA, 2022).

Although GR has been shown to impair aesthetics (Dhaliwal, Palwankar, Khinda, & Sodhi, 2012), lead to dentin hypersensitivity (Costa et al., 2014), increase the risk of root caries (Zhang et al. 2019) and impair oral health-related quality of life (Wagner et al., 2016), evidence on its prevention, as well as methods to control GA, are uncertain. Importantly, the dental care professional has the major role to provide oral hygiene advice based on the best

available evidence and, therefore, evidence-based findings concerning the characteristics of oral hygiene that would contribute more to the development of GA and/or GR must be established.

Previous meta-analyses of randomized controlled trials (RCTs) have investigated the risk of GR (Rajapakse et al. 2007; Van der Weijden et al. 2011; Heasman et al. 2015) and GA (Hoogteijling et al. 2017; Ranzan et al. 2018) comparing different types of toothbrushes. However, conventional pair-wise meta-analyses are designed to compare only head-to-head studies, and their results are limited to these direct comparisons. In light of this constraint, NMA has emerged as a suitable tool, providing comparative evidence for treatments not directly compared in a head-to-head RCTs (Chaimani et al. 2022). Therefore, this systematic review and NMA compared different morphologies/types of toothbrushes regarding the risk of GA and GR.

Material & Methods

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement extension for systematic reviews incorporating network meta-analyses (PRISMA-NMA) (Hutton et al., 2015) for reporting and Cochrane's standards for the methods of new Cochrane Intervention Reviews and Network Meta-Analysis (Higgins et al., 2019). This NMA was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with n° CRD42022326071.

PICOS Questions

Based on RCTs, what is the effect of toothbrushes with different types of arrangement and bristle finishing patterns (i.e., conical or end-rounded filament; flat; multisection bristles; or powered toothbrush) on the development of GA? (FQ1) and what is the effect of such devices on the occurrence of GR? (FQ2)

Selection criteria

The following inclusion criteria were used based on PICOTS process:

Patients (**P**): (1) systemically healthy adults (≥ 18 years old). Studies which participants had specific disorders (i.e.., autoimmune disorders, anorexia, bulimia) were not included.

Intervention/Comparator (I/C): RCTs comparing two or more of the following treatment modalities: 1) Toothbrushes with hard, medium or soft bristles; 2) Toothbrushes with different filament displays (e.g., flat or end-rounded filaments) and/or 3) Toothbrushes with different bristle heights and directions (e.g., flat-trimmed or multisection bristles); or Powered toothbrushes. RCTs that compared different commercial brands of toothbrushes having the same bristle's morphology were not included.

Outcomes (**O**): The difference in extent of GA and GR for FQ1 and FQ2, respectively, respectively. Data on the diagnosis of GA and GR was collected as determined by the primary study authors. Those studies with missing data or which the outcomes were presented differently were excluded.

Time (**T**): Studies with any follow-up time were considered for GA, and with at least six months of follow-up for GR.

Study design (S): Only RCTs.

Search Strategy

The following electronic databases were systematically searched up to 18 May 2022 with no language and date restrictions: MEDLINE (PubMed), EMBASE, Cochrane Register of Controlled Trials (Central), LILACS/BBO, and Web of Science. Grey literature was searched in clinical trials registers (Clinical Trials.gov), OpenGrey, and Google Scholar. Reference lists from the studies selected and previously published reviews (Rajapakse et al., 2007; Van der Weijden et al., 2011; Heasman et al., 2015; Hazan et al., 2018) were searched in an attempt to find records not retrieved during the electronic search. Full strategies for the databases are presented in the supplementary data (Appendix S2).

Selection of eligible studies and data collection

The Mendeley Desktop 1.19.4 (England) and Rayyan (Ouzzani et al., 2016) were used to remove any duplicates and to select the eligible studies from the databases and other sources (lists of references of included trials or grey literature), respectively. Previously to the application of selection criteria, reviewers (SSS and GBO) were pilot tested using 10 randomly selected studies to ensure consistency in the independent selection process. Inter-

observer agreement for the article's screening was assessed using the Kappa coefficient, which resulted in 0.92 for the screening of titles and abstracts and 0.94 for the full-text evaluation. Piloting for data extraction process was performed with the same systematic, but with two randomly selected studies. Any disagreement between reviewers on selection or data extraction process was resolved by consensus, and if not reached, by a third reviewer (FBZ).

Two independent reviewers (SSS and GBO) used a standardized and pilot-tested form based on Cochrane recommendations to extract relevant data on methods, participants, settings, interventions and outcomes.

The following data were extracted:

- Study characteristics: First author, year of publication, country, design, study period and funding;
- Sample characteristics: Total sample (N) at the beginning and at the end of the trial, age (mean and range), N of men and women, gingival biotype and eligibility criteria;
- Intervention protocols: characteristics of the toothbrush used by the participants (bristle type, brush brand, bristle design/cut, filament finishing); presence and type of dentifrice used (trademark, composition and abrasiveness [RDA]); brushing duration and daily frequency.
- Results and data analysis: Type of index used to assess each outcome and respective scores at baseline and the last study time-point.

Data analysis

Mean change (End – baseline) and standard deviation of changes for both GA and GR indices were extracted. Differences were calculated by subtracting the final from the baseline scores; and the standard deviation of changes, when not present, was calculated using the formula SD delta= $\sqrt{[(SD_1)^2+(SD_2)^2-(2*r*SD_1*SD_2)]}$ (Higgins et al. 2019), where SD₁ is the standard deviation of the baseline mean value and SD₂ is the standard deviation of the final mean value.

Traditional pairwise meta-analyses with random-effects models were performed using the DerSimonian and Laird estimator for inter-study variability (DerSimonian and Laird, 1986). Statistical heterogeneity was assessed in each paired comparison using the I² statistic and the Cochran test. Forest plots were created for all direct comparisons and the results were presented as mean changes (MD) and respective 95% confidence intervals (CI). Only a direct

analysis was performed with the risk ratio (RR) as effect measure, due to the presentation of the data in the primary studies.

Network meta-analyses (NMA) were performed integrating direct and indirect estimates for both GA and GR in order to compare all different interventions in a single model (Lu & Ades 2004). The network geometry was reported with a network plot, used to identify whether the different treatments were connected. The model uses a hierarchical Bayesian structure to compare multiple treatments through common comparators. The inference was performed using the Markov Chain Monte Carlo technique. For the present NMA, treatments were grouped into common nodes based on each agent. Therefore, for both outcomes, NMA were constructed based on 4 interventions: (1) Manual toothbrush with endrounded filaments (End); (2) Manual toothbrush with tapered filaments (Tap); (3) Manual toothbrush with multilevel bristles (Mtl); and (4) Powered toothbrush (PT).

Both fixed and random effects models with homogeneity of variances were fitted using minimally informative priors for all parameters. All models included four Markov chains with 180,000 iterations after an initial burn-in of 20,000 and a thinning of 150. The goodness of fit of the models was evaluated using residual deviation and deviation information criteria (DIC) to choose the best adjustment, this being the random model. Results from NMA were presented as a summary of relative effects sizes for each possible treatment in leaderboards as MD with respective 95% credibility intervals (CrI).

The estimated ranking probabilities for each treatment in the network to achieve a specific placement in an ordering of treatment effects, from best to worst, were reported as the surface under the cumulative ranking curve (SUCRA) (Hutton et al. 2015). All analyzes were performed using statistical software R, version 4.0.4 (meta, gemtc and rjags packages) (Schwarzer et al. 2010).

Risk of bias and assessment of reporting bias

Two independent reviewers (SSS and GBO) assessed the risk of bias using the Cochrane Risk-of-Bias tool for randomized trials version 2 (RoB 2.0) (Sterne et al., 2019) in RevMan (version 5.0 for Windows; Cochrane Collaboration, Oxford, UK). Each study was classified as "low risk of bias", "some concerns" or "high risk of bias" in the following domains: bias arising from the randomization process; bias due to deviations from the intended intervention; missing outcome data bias; bias in the measurement of results and bias in the selection of reported results, including deviations from the recorded protocol. We

classified as having an overall high risk of bias if one or more domains were classified as "high risk of bias". Low overall risk of bias was considered if all domains were classified as "low risk of bias". Studies were classified as "some concerns" when they have this result in at least one domain, but were not at high risk of bias for any other.

We planned to perform sensitivity analyzes to assess whether the study's risk of bias would affect the results excluding RCTs with a high risk of bias. However, this was not possible due to the small number of studies included in meta-analysis. Moreover, the assessment of publication bias and risk of bias between studies with an adjusted funnel plot for comparison was not possible due to the same reason.

Certainty of evidence

The certainty of evidence was assessed for each comparison using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach for NMA (Bonner et al., 2018; Brignardello-Petersen et al., 2018; Puhan et al., 2014; Schunemann et al. 2013) by the same two independent reviewers (SSS and GBO).

As only RCTs were eligible, NMA treatment effects were initially assigned a high confidence rating based on risk of bias, inconsistency, indirectness and publication bias, and rating levels included "serious", "very serious" or "no concerns". The risk of bias was reduced by one tier when the overall risk of bias was rated as "some concerns" and by two tiers when the overall risk of bias was rated as "high". Inconsistency was reduced if effect estimates varied between studies. Indirectness was downgraded if more than 30% of the combined estimated weight came from studies where populations had different characteristics (age, systemic condition).

Publication bias was reduced if industry funding leads to reporting a positive outcome favoring sponsored treatment (Martins et al. 2020). Then, the assessment of intransitivity was evaluated based on the two closest direct comparisons that contributed to each indirect comparison, and then the one with the least certainty of evidence was adopted.

It was planned to use a split-node technique to assess local inconsistency and obtain indirect estimates (Dias et al. 2010). However, for GA and GR the node split models were not allowed due to the star shape of the networks, therefore, as no pair of comparisons had direct and indirect evidence, we found no reason to downgrade due to inconsistency (Veroniki et al., 2013). The certainty of the evidence was classified as high, moderate, low and very low.

Results

Study selection

Regarding the electronic search in the databases and the manual search in the reference sections of relevant articles, 6251 articles were found. A total of 930 duplicate articles were excluded. Of the remaining 68 articles, 12 were included for the outcome GA and 9 for GR, 6 articles for GA and 7 articles for GR were included in the meta-analysis (Figure 1).

Study characteristics

Gingival Abrasions

Table 1 describes the main characteristics of the studies included for GA outcome. Considering the studies included in NMA, a total of 378 subjects were for outcome GA, most participants had some level of gingival bleeding, but without moderate to severe periodontitis. Follow-up ranged from 2 to 4 weeks in 4 of the 6 studies (Rosema et al. 2010; Versteeg et al. 2008; Hennequin-Hoenderdos et al. 2016; Mantokoudis et al. 2001) and most of them instructed volunteers to maintain their oral hygiene routine with 2 minutes twice-daily brushing their oral hygiene routine with twice-daily brushing and a duration of 2 minutes. Most studies used the method of Danser et al. (1998) to assess GA, which were dichotomized as small (≤ 5 mm) or large (> 5 mm).

Among the characteristics of toothbrushes, comparisons included toothbrushes which bristles presented round filaments ends (Rosema et al 2008; Mantokoudis et al 2001; Hennequin Hoenderdos et al 2016; Versteeg et al 2008; Rosema et al 2010; Caporossi et al 2015), tapered filaments (Caparossi 2013; Versteeg et al 2008; Hennequin-Hoenderdos et al. 2016), multilevel filaments (Rosema et al 2010), and power toothbrushes with oscillating movements (Mantokoudis et al. 2001; Rosema et al.2008). Considering pairwise comparisons, medium toothbrushes were evaluated in 5 studies (Greggianin et al. 2013; Zanatta et al. 2011; Zimmer et al. 2011; Romitti et al. 2021; Mantokoudis et al. 2001), and hard bristle toothbrush in one study (Zimmer et al. 2011).

Gingival Recessions

Table 2 shows the characteristics of the included studies for the GR outcome. A total of 521 subjects were included in the NMA. Follow-up times varied from 6 (Cecchin et al. 2007 Cifcibasi et al. 2014; Dentino et al 2002; Dofer et al. 2009) to 12 months (McCracken et al. 2009; Sälzer et al. 2016) for most studies. The study by Dorfer et al. 2016 had a 3-year follow-up, with the same subjects since the study by Dofer et al. 2009.

All studies considered as inclusion criteria participants with at least 2 mm of labial/buccal GR, which most of them calculated GR as the difference between CAL and PPD.

Among the characteristics of toothbrushes, all studies showed comparisons with brushes whose bristles had round filament tips, the studies by Cecchi et al. 2007 also evaluated brushes with conical filaments, Cifcibasi et al. (2014) with multilevel bristles and the other 5 studies compared with electric toothbrush (Dentino et al. 2002;Dorfer et al. 2016; Salzer et al. 2016;McCracken et al. 2009;Dofer et al. 2009)

Risk of bias

One study was at high risk of bias according to the RoB 2.0 assessment (Johnson et al. 1994), while five were at low risk. The risk of bias domains for all eligible studies and the overall risk of bias plot are shown in supplementary file (Fig S3).

Network structure presentation and network geometry summary

Graphical representations of networks for all available comparisons are shown in Fig. 2. All geometries had incomplete connections (loose ends instead of closed loops) because most treatments were not directly compared with each other. The width of the lines is proportional to the number of trials comparing each pair of treatments. The size of the nodes is proportional to the number of patients randomized to each toothbrush.

Synthesis of results

According to the pairwise results, there were no significant differences between manual and powered toothbrush as well as between end-round and tapered filaments for the GA outcome. The comparison between soft and medium toothbrush bristles, soft bristles significantly protected for GA [RR: 0.73 (CI 0.58;0.91); Fig S1D], whereas powered

toothbrush showed lower significant RG progression compared to manual toothbrushes [MD=-0.11 (CI -0.17; -0.04); Fig. S2B].

Fig. 3 shows the league table with NMA estimates. There were no significant differences between any comparison for both GA and RG outcomes. Regarding the probability of classification according to the SUCRA curves (Fig.4), for GA the best result was for powered toothbrushes (SUCRA=0.83), followed by end-rounded filaments (SUCRA=0.49). For GR, end-rounded filaments (SUCRA=0.71) was the first, followed by the toothbrushes with multilevel filaments (SUCRA=0.66).

Certainty of evidence

Estimates of certainty of evidence are presented in table 3. Overall, NMA certainly has evidence rated from low to very low.

Discussion

The absence of statistically significant differences between the compared interventions indicate that the characteristics of toothbrushes do not seem to be preponderant regarding the occurrence or progression of GA and/or GR, what confirmed the null hypothesis of this study. However, SUCRA findings indicated that manual toothbrushes with end-rounded bristles have a good balance for both outcomes, highlighting this toothbrush characteristic as the safest for preventing GA and GR development/progression.

The bristles determine not only the durability, but also the ideal flexibility that allows an efficient dental plaque control without damaging the oral tissues (Zaze et al., 2016) and, given these aspects, are considered the most important components of the toothbrushes. According to the American Dental Association (ADA), the ideal toothbrush must present some specific characteristics in order to improve the efficacy of plaque control, such as endrounded nylon bristles with the equal length, small head and shaft located at the same axis, lightness and ease of cleaning, impermeability to moisture, low cost and durability.

Our results from direct comparisons showed that toothbrushes with soft bristles are protective for GA when compared to medium bristles, corroborating with systematic review by Razan et al. (2018) who concluded that soft brushes tend to be safer than hard and medium ones to avoid GA. Unfortunately, it was not possible to add medium bristles in our NMA, due to the way the results from primary studies were collected and reported. Even so, we can

conclude that toothbrushes with medium or hard bristles should be avoided and not recommended. Regarding toothbrush filaments, our results indicated that there is no differences between conical and rounded filaments considering GA outcome, which corroborates previous evidence (Hoogteijling et al. 2017; Hazan et al. 2018). In addition, our data showed that these two characteristics it seems both types of filaments are similar considering the risk for GR development/progression.

Our results from direct evidence and from NMA identified that PT are at least as safe as manual toothbrushes for GR development/progression. These results corroborates previous pairwise meta-analysis (Van der Weijden et al., 2011; Heasman et al. 2015), including the latest Cochrane update from Yacob et al. (2014), which reported its safety for GR, with higher efficacy of dental biofilm removal and gingival inflammation control than manual toothbrushes. The SUCRA's results from power toothbrushes was contradictory, as best ranked for GA and worst for GR. The high variability (high SDs levels) in GR outcome can possibly explain these results. Even so, we can feel secure to recommend PT for dental hygiene. Currently, PT with a generation linked to technology, which the advanced models incorporated new oscillating innovations and/or sound-based technology, probably helps to increase toothbrushing motivation in relation to manual toothbrushes (Van der Weijden et al. 2011), but their disadvantage is still the high cost (Walters et al. 2007). Thus, its recommendation should take into account the patient's financial profile.

Limitations

In our study, few RCTs were eligible, which is a limitation regarding the reliability of the findings. Furthermore, the clinical interpretation of the NMA results is limited not only by the small number of trials at each node, but also because the networks are star-shaped and poorly connected, depending largely on indirect comparisons. All comparisons were low or very low, certainly resulting in uncertainty around the estimates. Therefore, the results of this NMA should be interpreted with caution.

To ensure a broader inclusion of primary studies, we have not established a minimum follow-up, so follow-up times (1 brushing episode and follow-up of up to 3 years) can be a source of heterogeneity, making direct comparison of primary studies difficult. Also, many studies did not present AG and GR as the main outcome, and a lot of bias was found in terms of selective outcome reporting. It should also be noted that 11 studies reported financing by private companies (Versteeg et al. 2008; Hennequin-Hoenderdos et al. 2016; Mantokoudis et

al. 2001; Rosema et al. 2008; Salzer et al. 2015; Cecchin et al. 2015; Cecchin et al. 2007; Dentino et al. 2002; Dorfer et al. 2016; Sälzer et al. 2016; McCracken et al. 2009; Dofer et al. 2009). Therefore, the shortcomings detected in the present study underscore the need for further research based on well-designed RCTs, particularly with direct comparison, to provide reliable estimates of the effect of toothbrush characteristics on gingival tissues.

Clinical recommendations

Soft end-rounded bristle toothbrushes seem to be the best option when there is interest in GA and/or GR prevention. However, other oral hygiene characteristics not analyzed in the present review also demonstrate relevance, such as brushing frequency, duration, pressure and technique – variables previously listed with potential to increase the risk of GR (Rajapakse et al. 2007; Heasman et al. 2015). In addition, thin gingival biotype (Cortellini & Bissada, 2018) and psychosocial factors (i.e., anxiety and stress) should also be taken into consideration. Lastly, we must reinforce that the devices compared in our NMA did not present different effect sizes, meaning the preponderant seems to be the individual profile and behaviour when toothbrushing.

Conclusion

Considering the limitations of this NMA, our results support that soft toothbrushes with rounded filaments is the best toothbrush characteristic to avoid both for GA and GR. However, among the different options of soft toothbrushes, the different characteristics seems to have little effect over GA and GR.

Fig. 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources. From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: https://doi.org/10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

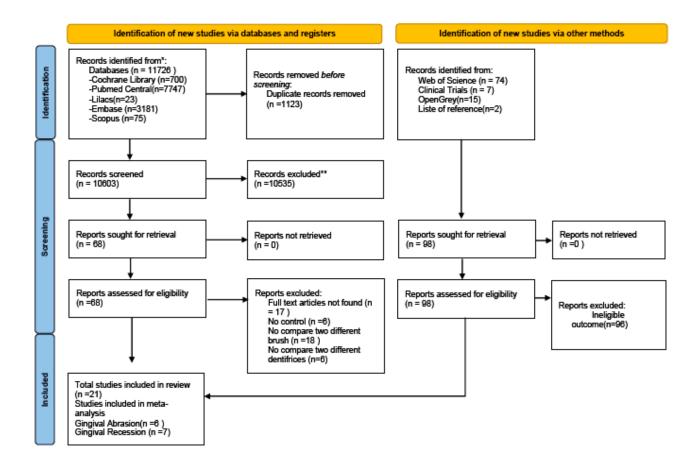


Fig.2 Network plot geometry for GA and RG. Nodes and edges weighed according to the number of studies involved in each comparison.

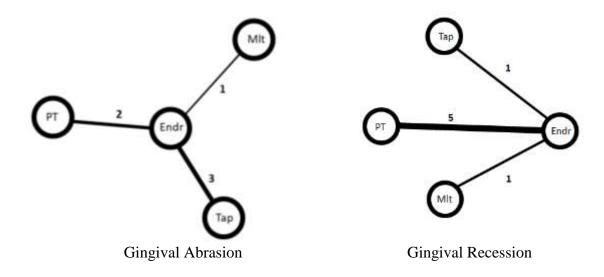


Fig.3 League table showing network meta-analysis results for Gingival Abrasion and Gingival Recession

	Endr	Тар	PT	Mtl
PT	PT	0.292 (-1.007, 1.717)	-0.974 (-2.815, 1.088)	0.492 (-3.468, 2.586)
Тар	0.07 (-0.119, 0.262)	Тар	-1.288 (-3.662, 1.233)	0.18 (-3.019, 3.424)
Elet	0.074 (-0.017, 0.175)	0.004 (-0.206, 0.213)	PT	1.414 (-4.978, 2.026)
Mtl	-0.189 (-1.236, 0.855)	-0.259 (-1.318, 0.812)	0.258 (-0.8, 1.314)	Mtl

Data should be read from left to right: MD (95% CrI) for Gingival Abrasion (GA) (upper triangle, orange) and MD (95% CrI) for gingival recession (GR) (lower triangle, blue). For GA, a MD below 0 favours the row-defining treatment. For GR a MD below 0 favours the column-defining treatment. Significant results are shown in bold. CrI=credible interval. MD= mean difference. Endr=end round filaments Tap=tapered conical filaments. PT=Power toothbrushes. Mtl=Multilevel tufs.

Fig.4 The ranking of treatments based on surface under the cumulative ranking curve (SUCRA).

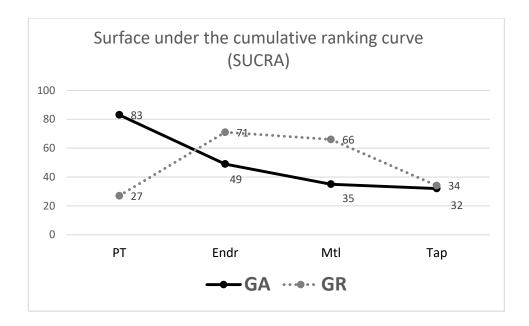


Table 1 – Overview of the studies included to address FQ1.

First author, Year/ Country	Design Duration Funding	N: Baseline (end) M (N) / F (N) Age mean Age Range Gingival Biotype	Eligibility criteria	Intervention Bristle type Brush brand Bristle design/cut Filament finishing	Dentifrice RDA Quantity of dentifrice Time of TB Times of daily TB	Gingival Abrasion measure	Overall RoB 2.0
Caporossi et al. (2016) Brazil	 1 episode of toothbrushing; Funding: No funding	• 39 (39) • M (18) / F (21) • 23.5 (2.66) • NR • NR	 Papilla completely filling the interdental space; ≥ 24 teeth; ≤ 15% of sites with BoP; 	(A)Soft manual brushes (Colgate 360° deep clean®) Flat-trimmed Tapered (B)Soft manual brushes Oral-B indicator PLUS® Flat-trimmed End-rouded	 Stannous fluoride dentifrice (Oral-B Pró-Saúde RDA± 160 ±0.5 g 2 min Not applicable (only one episode of TB) 	Method of Danser et al. (1998) Small (≤ 5 mm) and large (>5 mm)	Low risk
Greggianin et al. (2013) Brazil	Wash-out of 10 days between two 28-days periods 11 examination sessions Funding: No funding	• 41 (35) • M (20)/ F (15) • 15.2(1.0) • 14 and 20 years old • NR	• ≥ 20 teeth • No history of destructive periodontal disease no gingival bleeding • No recession loss ≥2 mm	(A)Soft manual brushes (Sorriso Original Kolynos, Colgate) NR End-rouded (B)Medium manual brushes (Sorriso Original Kolynos, Colgate NR End-rouded	Non-therapeutic fluoride containing toothpaste (Sorriso Dentes Brancos, Colgate, EUA) RDA: NR No attempt was made to modify the oral hygiene habits of the participants.	Were considered vertical lesions departing from the gingival margin in an apical direction	Some concerns
Zanatta et al. (2011) Brazil	1 episode of toothbrushing Funding: No funding	 25 (25) M (18)/ F (7) NR 18 and 30 years GNR 	• Good/excellent systemic health • ≥ 20 teeth sites with attachment	(A) Soft manual brushes (Condor; São Bento do Sul, SC, Brazil) NR End-rouded (B) Medium manual brushes (Condor; São Bento do Sul, SC, Brazil) NR End-rouded	 Colgate triple action, Colgate-Palmolive; Santiago, Chile; RDA: NR NR 2 min Not applicable (only one episode of TB) 	Method of Danser et al. (1998)	Low risk

Zimmer et al. (2011) Germany	• 8 weeks • Funding: GlaxoSmithKline ConsumerHealthcare,Buh 1,Germany	 120 (NR) M (55)/ F (65) 36,3 (NR) 18 and 62 years NR 	•Healthy volunteers •≥ 16 teeth •No pregnant, diabetes, severe periodontal disease, used antibiotics, had removable dentures.	(A) Soft manual brushes (B) Medium manual brushes (C) Hard manual brushes (Best Plus toothbrush GlaxoSmithKline, Germany) NR NR	Best Multi Aktiv-Zahncreme, GlaxoSmithKline, Buhl, Germany RDA:NR NR NR 2 min Twice a day	Method of Danser et al. (1998)	Low risk.
Rosema et al. (2010) The Netherlands	• 2 weeks • Funding: No funding.	• 36 (35) • M (NR)/ F (NR) • : NR • NR • NR	• ≥ 18 years of age, • ≥ 20 teeth; • Absence of generalized gingival recession, and/ or PD>5 mm	(A) Soft manual brushes (Profit-Haije-Brush) Multi-level - U-shape design NR (B) Soft manual brushes (ADA reference) Flat-trimmed End-rouded	 Zendium_ frismint, Sara Lee H&BC, Veenendaal, The Netherlands). RDA ±76 NR 2 min Twice a day 	Method of Danser et al. (1998)	High risk
Versteeg et al. (2008) The Netherlands	• 4 week • Funding: GABA International, Münchenstein, Suíça	• 35 (32) • M (9)/ F (23) • 24(NR) • 21-42 • NR	• ≥ 20 teeth; • No smokers, oral lesions and or PD >5 mm; • ≤ 25% of sites with BoP;	(A) Soft Manual brushes Meridol® (GABA Intl., AG, Switzerland) NR Tapered (B) Soft manual brushes (ADA reference) Flat-trimmed End-rouded	Standard dentifrice (Everclean, Hema, Amsterdam, The Netherlands).] RDA: NR NR Twice a day	Method of Danser et al. (1998)	Some concerns
Hennequin-Hoenderdos et al. (2016) The Netherlands	4 week Funding: Procter & Gamble	• 50 (46) • M (14)/ F (32) • 22.5 ± 2.51 • 18–31 • NR	• ≥18 years of age, in good general physical and oral health, • ≥ 20 teeth	(A) Soft manual toothbrushes (Oral-B) NR 0% end-rounded = Tapered (B) Soft manual toothbrushes NR 40–50% end-rounded filaments (C) Soft manual brushes (ADA reference) Flat-trimmed End-rouded (90%)	 Fluoride toothpaste, 1450 NaF. (Oral-B) RDA: NR NR NR Twice a day 	Small (≤ 2.5 mm), medium (≥ 2.5 but ≤ 5 mm) and large (>5 mm)	Low risk
Romitti et al. (2021)	6 months Funding: No funding.	• 20(17) • M (6)/ F (14) • 18.9 ± 2.5 • 14 and 24 years • NR	Good/excellent systemic health No history of periodontitis and NIC ≥ 3 mm	(A)Soft manual brushes (Sorriso Original, Colgate-Palmolive®, São Paulo, SP, Brazil). Multi level End-rouded (A)Medium manual brushes (Sorriso Original, Colgate-Palmolive®, São Paulo, SP, Brazil). Multi level End-rouded	Non-therapeutic MFP-toothpaste (Sorriso Dentes Brancos) g, Colgate-Palmolive®, São Paulo, SP, Brazil). NR NR NR NR NR	Whenever a V-shaped notch or groove-shaped lesion is detected, regardless of size, located on the gingival margin on the buccal surfaces.	
Mantokoudis et al. (2001) Berne, Switzerland	3 experimental phases of 2 weeks design with a wash-out of 7 days Funding: Braun Oral- B, Germany	• 26 (24) • M (16)/ F (10) • 25 • 23 and 41 years • NR	Good general health No supragingival calculus, medication taken within the last 28 days, or allergies to test products.	(A)Braun Oral-B Plak Control Ultra. 7600, oscillating movements/min (EB 15, Braun GmbH, Germany). (B) Braun Oral-B Plak Control 3D 20,000 movements/ Min (C) Medium manual brushes Paro M® (ESRO AG,CH-8880 Thalwil) Flat-trimmed End-rouded	 Mentadent C sensitive (Elida Faberge CH-Zug) RDA± 62; NR 2 min Twice a day 	Method of Danser et al. (1998)	Low risk

Danser et al. (1998) The Netherlands	• 3 weeks • Funding: No funding.	 50 (47) M (NR)/ F (NR) NR NR NR 	• Minimum of 6 teeth in each of the 4 quadrants and no pockets >4 mm.	(A) Braun Oral-B <i>Ultra</i> Plaque Remover® (D9) (B) Soft manual brushes (Butler 411®) Square U-shape design NR	 Fluoride toothpaste (Zendium®) RDA±60 NR 2 min NR 	Method of Danser et al. (1998)	Some concerns
Rosema et al.(2008) The Netherlands	• 9 months • Funding :Procter & Gamble	• 122 (114) • M (22)/F (92) • 22 years • NR • NR	•≥ 18 years of age, •≥ 20 teeth; No oral lesions and/or DP >5 mm, BOP >40%	(A) Electric Toothbrush: Oral-B Triumph Professional Care 9000 (D25) (B) Soft manual brushes (ADA reference) Flat-trimmed End-rouded	 Standard (NaF) Zendium frismint RDA: 76 NR 2 min Twice a day 	Method of Danser et al. (1998)	Some concerns

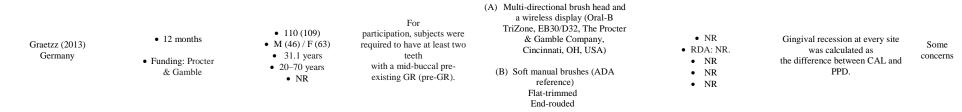
RCT: randomized clinical trial; N: Number of subjects; M: masculine; F: feminine; TB: toothbrush; NR: not reported; SLS: sodium lauryl sulfate; RDA: relative dentin abrasion score; ADA: American Dental Association; NRCT: Non-Randomized clinical trial; BOP: bleeding on probing; PD: probing depth; CAL: attachment loss; GB: Gingival Biotype.

Table 2 - Overview of the studies included to address FQ2 N: Baseline (end) Intervention Dentifrice Design/ M(N)/F(N)Bristle type RDA Overall RoB First author, Eligibility Duration Age mean **Brush brand** Quantity of dentifrice Gingival recession measure 2.0 Year/ Country criteria Funding Age Range Bristle design/cut Time of TB **Gingival Biotype** Filament finishing Times of daily TB (A) Soft manual brushes (Meridol ®) • 30 (30) A sensor probe was used NR • M (14) / F (16) Tapered during the clinical examination • 6 months • RDA: NR Without either periodontitis Cecchin et al. (2007) • M 21.8 (1.15)/ F 21.7 (PDTSensor Probe Type Roy Low risk or history of periodontal • NR. Italy (B) Soft manual brushes (ADA • Funding: GABA (1.12)/STM) surgery 2 min International AG NR reference) Number and width of gingival · twice a day Flat-trimmed recession were recorded • NR End-rouded (A) Soft manual brushes (Oral-B Indicator, 35-soft, P and G, · With no antiplaque agent • 40 (35) Good general and oral Istanbul, Turkey) (Ipana Classic Taste, P and G, Gingival recession at every site • (15) / F (25) Flat-trimmed Istanbul, Turkey) Cifcibasi et al. (2014) health; • 6 months was calculated as Low risk • RDA: NR Turkiye • 23-25 years a minimum 6 teeth End-rouded the difference between CAL (B) Soft manual brushes CrissCross® no PD ≥3 mm or CAL≥2 • NR. Funding: NR NR and PPD. (Oral-B®) • NR mm. NR Multi-level · twice a day End-rouded • (A) Oscillating-rotating powered • 172 (157) · Fluoride toothpaste (Crest, toothbrush Gingival recession at every site • M (53) / F (104) · Mild to moderate Some Dentino et al (2002) • 6 months (B) Soft manual brushes (ADA Procter & Gamble). RDA: NR. was calculated as • 31.8 gingivitis $\bullet \ge 20$ teeth; concerns • NR. United States • Funding: Braun/Oral B reference) the difference between CAL and • 18-61 Flat-trimmed • 2 min PPD.. • NR

End-rouded

· twice a day

Dorfer et al (2016) Germany	• 3 years • Funding: Procter & Gamble	 109 (75) M (39) / F (36) Groups - Manual 32.2 (8.9) and power 33.6 (10.2) NR NR 	Good general health ≥ 20 teeth; Two or more teeth showing recession on the facial surface of at least 2 mm.	(A) oscillating–rotating and pulsating power brush (D17U, Oral-B ProfessionalCare, Procter & Gamble) (B) Soft manual brushes (ADA reference) Flat-trimmed End-rouded	Standard sodium fluoride dentifrice (Blend-a-Med; Procter & Gamble). RDA: NR. NR 2 min twice a day	Gingival recession at every site was calculated as the difference between CAL and PPD.	Low risk
Sälzer et al (2016) Germany	12 months • Funding: Procter & Gamble	• 110 (55) • M (47) / F (63) • 31.0±11.2 • NR • NR	• ≥ 20 teeth; • Two or more teeth showing recession on the midbuccal surfaces of at least 2 mm.	(A) Multi-directional power toothbrush (5000 model, EB30/D32, Oral-B, Procter & Gamble) (B) Soft manual brushes (ADA reference) Flat-trimmed End-rouded	Standard sodium fluoride dentifrice (Blendax Anti-Belag; Procter & Gamble). RDA: NR. NR In NR In twice a day	GR calculated as the difference of CAL and PPD. Analysis of differences in the magnitude of gingival recession (Hmax).	Low risk
Johnson et al., (1994) United States	• 6 months • Funding: Optiva Corporation, Bellevue, WA.	 51 (29) Groups - Manual 30.5 and sonic 32.3 Groups - Manual 20-50 and sonic 20-54 NR 	• ≥ 20 teeth; • Exhibit a mean Gingival Index13 of at least 1.5 on the six Ramfjord teeth	(A) Sonic toothbrush (Sonicare, Optiva Corp., Bellevue, WA) (B) Manual toothbrush (Oral B 30, Redwood City, CA) NR NR	Standard brand toothpaste (Crest regular, Procter & Gamble). RDA: NR. NR. In twice a day	Assessed as recession of 0.5 mm or greater.	High risk
McCracken et al., (2009) United Kingdom	• 12 months • Funding: Philips Oral Healthcare, WA, USA	• 60 (52) • Groups - Manual 27(8) and powered 24(5) • NR • GB: NR	Good/excellent health Localized areas of buccal/labial GR with at least CAL= 1mm	(A) Powered toothbrush (Philips Sonicare Elite, WA, USA) (B) Soft Manual toothbrus (Oral B 35, Proctor & Gamble, Surrey, UK) NR End-rouded	Standard brand toothpaste (Crest regular, Procter & Gamble) RDA: NR. NR. 2 min twice a day	Target teeth with localized gingival recession were identified. The recession defect was classified according to Miller (1985).	Low risk
Dofer et al.(2009) Germany	• 6 months • Funding: Procter & Gamble	• 109 (106) • M (51) / F (55) • 33 years • NR • NR	General healthy adults with ≥2 teeth with facial recession ≥2 mm; ≥18 scorable teeth.	(A) Oral-B Professional Care 7000 (D17); (The Procter & Gamble Company, Cincinnati, OH, USA (B) Soft manual brushes (ADA reference) Flat-trimmed End-rouded	Sodium fluoride dentifrice (Blend-a-Med®; The Procter & Gamble, OH, USA). RDA: NR. NR 2 min twice a day	Gingival recession at every site was calculated as the difference between CAL and PPD.	Low risk



RCT: randomized clinical trial; N: Number of subjects; M: masculine; F: feminine; NR: not reported; RDA: relative dentin abrasion score; ADA: American Dental Association; NRCT: Non-Randomized clinical trial; BOP: bleeding on probing; PD: probing depth; CAL: attachment loss; GB: Gingival Biotype.

Table. 3 Certainty of evidence and reason for downgrading.

Certainty of evidence	Reason for downgrading
Very Low	Study limitation – Imprecision.
Very low	Study limitation – Risk of bias ^a ; Imprecision ^b .
Low	Study limitation – Risk of bias ^a ; Imprecision ^b .
Very Low	Study limitation – Risk of bias ^a ; Imprecision ^b .
Low	Study limitation – Risk of bias ^a ; Imprecision ^b .
Very Low	Study limitation – Risk of bias ^a ; Imprecision ^b .
	Very Low Very low Low Very Low Low

toothbrush

a The risk of bias was reduced by one notch when the overall risk of bias was rated as "some concerns"; b Downgraded by two levels; due to imprecision: the CrI is wide and includes zero reflecting the uncertainty around the direction of effect.

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SUPPLEMENTARY DATA

Are the type and morphology of toothbrushes important for gingival abrasion and gingival recession prevention? A Systematic Review and Network Meta-analyses

Appendix S1. PRISMA Checklist of Items to Include When Reporting a Systematic Review Involving a Network Meta-Analysis (NMA)

Appendix S2. Search Strategy in the Cochrane Library, MEDLINE/PubMed (via National Library of Medicine), Embase, Scopus and Web of science, and Cochrane Appendix S3. The certainty of evidence produced by the synthesis for each outcome, assessed through GRADE approach for network meta-analysis (NMA)

Figure S1. Pairwise Meta-analysis Results: Gingival Abrasion

Figure S2. Pairwise Meta-analysis Results: Gingival Recession

Figure S3. Risk of bias assessments (ROB2 risk of bias domains for all eligible trials and overall risk of bias graph)

Figure S4. Forestplot comparing all treatments for GA.

Figure S5. MCMC simulation for GA outcome

Figure S6. Forestplot comparing all treatments for GR.

Figure S7. MCMC simulation for GR outcome

Appendix S1. PRISMA Checklist of Items to Include When Reporting a Systematic Review Involving a Network Meta-Analysis (NMA)

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review incorporating a network meta-analysis (or related form of meta-analysis).	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: Background: main objectives Methods: data sources; study eligibility criteria, participants, and interventions; study appraisal; and synthesis methods, such as network meta-analysis. Results: number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity. Discussion/Conclusions: limitations; conclusions and implications of findings. Other: primary source of funding; systematic review registration number with registry name.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, <i>including mention of why a network meta-analysis has been conducted</i> .	3
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			3
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. <i>Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).</i>	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6

Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Geometry of the network	S1	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	7
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.	7
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • Handling of multi-arm trials; • Selection of variance structure; • Selection of prior distributions in Bayesian analyses; and • Assessment of model fit.	7
Assessment of Inconsistency	S2	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • Alternative formulations of the treatment network; and	

• Use of alternative prior distributions for Bayesian analyses (if applicable).

RESULTS†

RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Presentation of network structure	S 3	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	11
Summary of network geometry	S4	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	11
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. <i>Modified approaches may be needed to deal with information from larger networks</i> .	10
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. <i>In larger networks, authors may focus on comparisons versus a particular comparator</i> (e.g. placebo or standard care), with full findings presented in an appendix. <i>League tables and forest plots may be considered to summarize pairwise comparisons.</i> If additional summary measures were explored (such as treatment rankings), these should also be presented.	11
Exploration for inconsistency	S5	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, <i>P</i> values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses, and so forth).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any	14

		concerns regarding network geometry (e.g., avoidance of certain comparisons).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16
FUNDING Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	1

Appendix S2. Search Strategy in the Cochrane Library, MEDLINE/PubMed (via National Library of Medicine), Embase, Scopus and

Web of science, and Cochrane

Search strategy performed in all databases. (November 02, 2021)

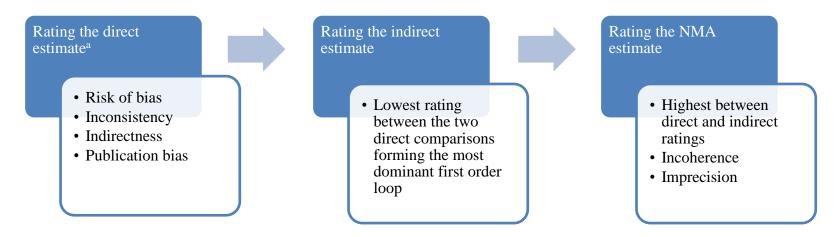
Database	Number	Search strategy
	of studies	
	studies retrieved	
PubMed	7747	#1 - (((Toothbrushing [MeSH Terms]) OR (Tooth brushings)) OR (Toothbrushes)) OR (Dental Devices, Home Care [MeSH Terms])) OR (Oral hygiene[MeSH Terms])) OR (manual toothbrush)) OR (Dental Hygiene)) OR (Bristle)) OR (Round brush)) OR (Conical brush)) OR (end-rounding)) OR (filament)) OR (tapered)) OR (toothbrush filament)) OR (toothbrush design)) OR (toothbrush bristle)) OR (toothbrush bristle)) OR (Soft Toothbrushes)) OR (Medium Toothbrushes)) OR (Bristle)) OR (Soft Toothbrushes)) OR (Medium Toothbrushes)) OR (Bristles)) OR (Butler 411 brush)) OR (Oral-B 35 Advantage)) OR (Jordan V-shaped, medium)) OR (Condor Toothbrush)) OR (Jordan V-shaped, medium)) OR (Condor Toothbrush)) OR (Oral B 404)) OR (Oral B Advantage B35)) OR (Close Up Deep Clean)) OR (Colgate diamond headed)) OR (Colgate Actibrush)) OR (Butler gum (Elmex Super 29)) OR (Power toothbrush)) OR (Powered Brushes)) OR (Socillating Toothbrushing)) OR (rotating Toothbrushing)) OR (Philips Jordan)) OR (Philips Jordan) OR (Philips Jordan) OR (Philips Jordan Sensiflex)) OR (Philips Jordan 2-action Plaque Remover)) OR (Philips HP555)) OR (Philips HP510)) OR (Braun D91) OR (Brau
		#2 - (((((((((((((((((((((((((((((((((((
Embase	3181	('tooth brushing'/exp OR 'brushing, dental' OR 'brushing, tooth' OR 'dental brushing' OR 'tooth brushing' OR 'toothbrushing' OR 'electric toothbrush'/exp OR 'unico (device)' OR 'electric toothbrush' OR 'electric toothbrushes' OR 'powered toothbrush' OR 'toothpaste'/exp OR 'crest mint' OR 'crest regular' OR 'dental powder' OR 'dentifrice' OR 'dentifrice' OR 'fresh breath' OR 'gleam' OR 'graigmartin' OR 'iodent' OR 'maclean' OR 'macleans' OR 'orabase (drug)' OR 'plus white' OR 'sensodyne' OR 'toothpaste' OR 'toothpaste' OR 'toothpaste' OR 'ultrabright' OR 'walgreen' OR 'worthmore' OR 'or oral

		toothbrushes' OR dentifrices OR 'relative dentin abrasivity' OR 'rda dentifrice') AND ('gingiva disease'/exp OR 'exfoliation, tooth' OR 'gingiva disease' OR 'gingiva recession' OR 'gingival diseases' OR 'gingival recession' OR 'inflammation, tooth crown 'OR 'pericoronitis' OR 'tooth crown inflammation' OR 'tooth exfoliation' OR 'abrasion'/exp OR 'abrasion' OR 'exposed root' OR 'gingival trauma' OR 'gingival retraction' OR 'gingival lesion') ('tooth brushing'/exp OR 'brushing, dental' OR 'brushing, tooth' OR 'dental brushing' OR 'tooth brushing' OR 'toothbrushing' OR 'electric toothbrush'/exp OR 'unico (device)' OR 'electric toothbrush' OR 'electric toothbrushes' OR 'powered toothbrush' OR 'toothpaste'/exp OR 'crest mint' OR 'crest regular' OR 'dental powder' OR 'dentifrice' OR 'dentifrice' OR 'fresh breath' OR 'gleam' OR 'graigmartin' OR 'iodent' OR 'maclean' OR 'macleans' OR 'orabase (drug)' OR 'plus white' OR 'sensodyne' OR 'thermodent' OR 'tooth paste' OR 'toothpastes' OR 'toothpastes' OR 'ultrabright' OR 'walgreen' OR 'worthmore' OR 'or oral hygiene' OR 'manual toothbrush'/exp OR 'toothbrush design' OR 'toothbrush filament' OR 'soft toothbrushes' OR 'medium toothbrushes' OR 'hard toothbrushes' OR dentifrices OR 'relative dentin abrasivity' OR 'rda dentifrice') AND ('gingiva disease'/exp OR 'exfoliation, tooth' OR 'gingiva disease' OR 'gingiva recession' OR 'gingival recession' OR 'gingival retraction' OR 'gingival lesion')
Cochrane Library	700	#1 - (((Toothbrushing [MeSH Terms]) OR (Tooth brushings)) OR (Toothbrushes)) OR (Toothbrush)) OR (brush)) OR (Dental Devices, Home Care [MeSH Terms])) OR (Oral hygiene[MeSH Terms])) OR (manual toothbrush)) OR (Dental Hygiene)) OR (Bristle)) OR (Round brush)) OR (Conical brush)) OR (end-rounding)) OR (filament)) OR (end-form)) OR (tapered)) OR (toothbrush lesign)) OR (Bristle)) OR (toothbrush bristle)) OR (tapered filament)) OR (end-rounding filament)) OR (toothbrush bristles)) OR (Bristle Stiffness)) OR (Soft Toothbrushes)) OR (Medium Toothbrushes)) OR (hard Toothbrushes)) OR (medium bristles)) OR (Hard bristles)) OR (Butler 411 brush)) OR (Oral-B 35 Advantage)) OR (Jordan V-shaped, medium)) OR (condor Toothbrush)) OR (Jondan V-shaped, medium)) OR (condor Toothbrush)) OR (Oral B 400) OR (Oral B 355)) OR (Close Up Deep Clean)) OR (Colgate diamond headed)) OR (Colgate Actibrush)) OR (Butler gum 311)) OR (Elmex Super 29)) OR (Power toothbrush)) OR (Powered Brushes)) OR (Postlating Toothbrushing)) OR (Philips Jordan)) OR (Philips Jordan 2-action)) OR (Braun Oral-b)) O
LILACS	23	#3 - #1 AND #2 (((((((((((((((((((((((((((((((((((

		Atrophy) OR (Gingiva Atrophies) OR (Atrophy of Gingiva) OR (Recessions, Gingival) OR (Recession, Gingival) OR (Gingival Recessions) OR (gingival abrasion) OR (Gingival erosion) OR (Gingival fissure) OR (Gingival trauma) OR (gingival ulceration) OR (Gingival lesion) [Words]
Scopus	75	
Web of	74	(Gingival recession OR Gingival abrasion) AND (Toothbrush)
Science		
Clinical	7	(Gingival recession OR Gingival abrasion) AND (Toothbrush)
Trials		
Open	15	(Gingival recession OR Gingival abrasion) AND (Toothbrush)
Grey		

Appendix S3. The certainty of evidence produced by the synthesis for each outcome

Criteria used to assess the certainty of evidence through GRADE approach for network meta-analysis (NMA) 1,2,3,4



^a Starting with high evidence (randomized controlled trials)

¹Bonner A, Alexander PE, Brignardello-Petersen R, Furukawa TA, Siemieniuk RA, Zhang Y, Wiercioch W, Florez ID, Fei Y, Agarwal A et al. 2018. Applying GRADE to a network meta-analysis of antidepressants led to more conservative conclusions. J Clin Epidemiol. 102:87-98.

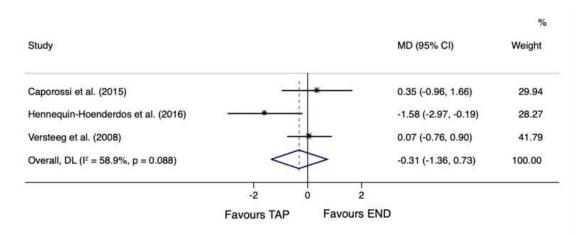
²Brignardello-Petersen R, Bonner A, Alexander PE, Siemieniuk RA, Furukawa TA, Rochwerg B, Hazlewood GS, Alhazzani W, Mustafa RA, Murad MH et al. 2018a. Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis. J Clin Epidemiol. 93:36-44.

³Martins CC, Firmino RT, Riva JJ, Ge L, Carrasco-Labra A, Brignardello-Petersen R, Colunga-Lozano LE, Granville-Garcia AF, Costa FO, Yepes-Nuñez JJ, Zhang Y, Schünemann HJ. Desensitizing Toothpastes for Dentin Hypersensitivity: A Network Meta-analysis. J Dent Res. 2020 May;99(5):514-522. doi: 10.1177/0022034520903036. Epub 2020 Feb 8. PMID: 32037944.

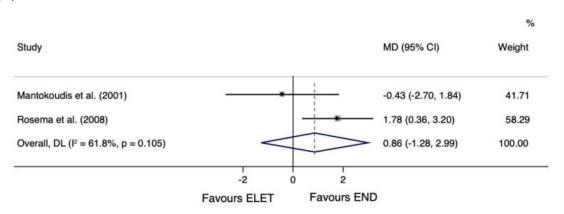
⁴Puhan MA, Schünemann HJ, Murad MH, Li T, Brignardello-Petersen R, Singh JA, Kessels AG, Guyatt GH; GRADE Working Group. A GRADE Working Group approach for rating the quality of treatment effect estimates from network meta-analysis. BMJ. 2014 Sep 24;349:g5630. doi: 10.1136/bmj.g5630. Erratum in: BMJ. 2015;350:h3326. PMID: 2525273

Figure S1. Pairwise Meta-analysis Results: Gingival Abrasion

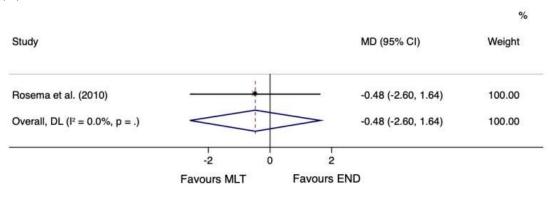
(A)



(B)



(C)





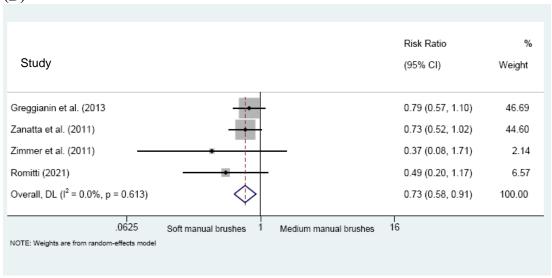
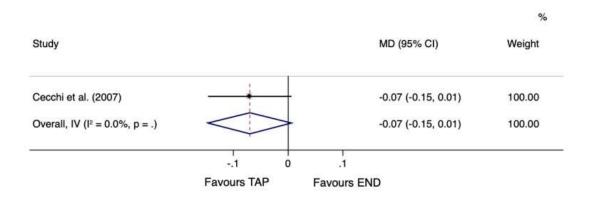
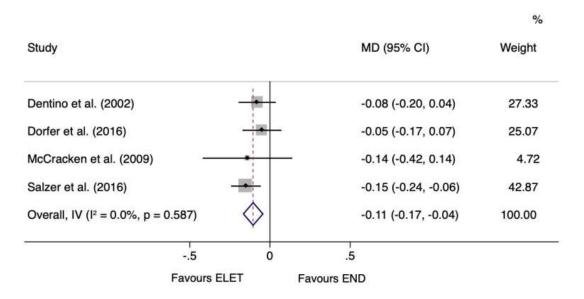


Figure S2. Pairwise Meta-analysis Results: Gingival Recession

(A)



(B)



(C)

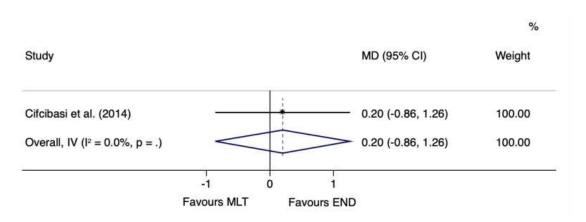
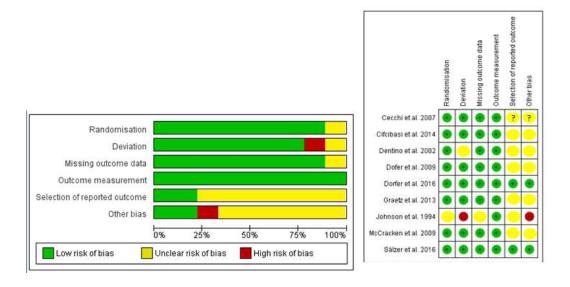
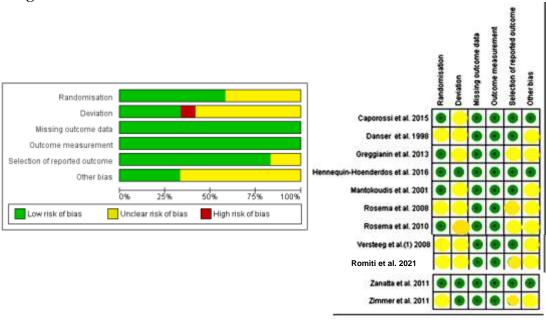


Figure S3. Risk of bias assessments

A) Risk of bias domains for all eligible trials according to Cochrane's RoB2

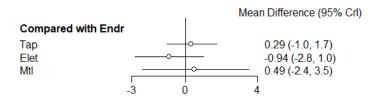


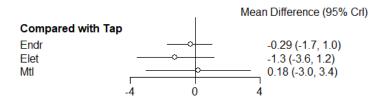
Gingival Recession



Gingival Abrasion

Figure S4. Forest plot comparing all treatments for GA.





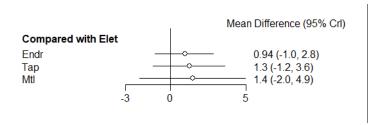
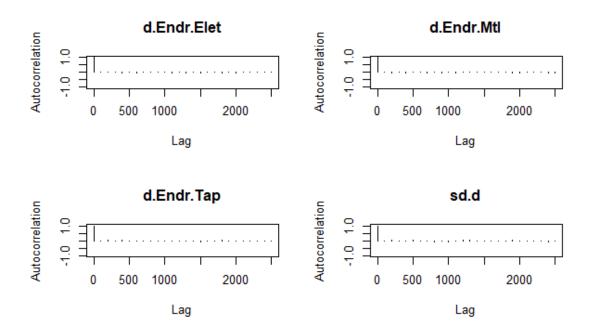


Figure S5. MCMC simulation for GA outcome



Traceplot

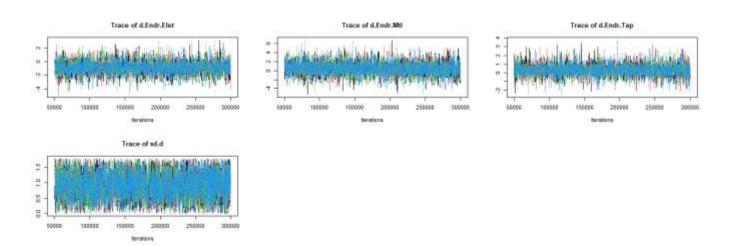
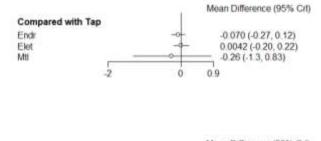
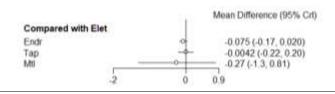
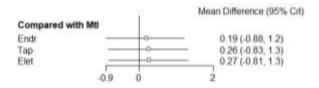


Figure S6. Forestplot comparing all treatments for RG.







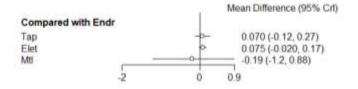
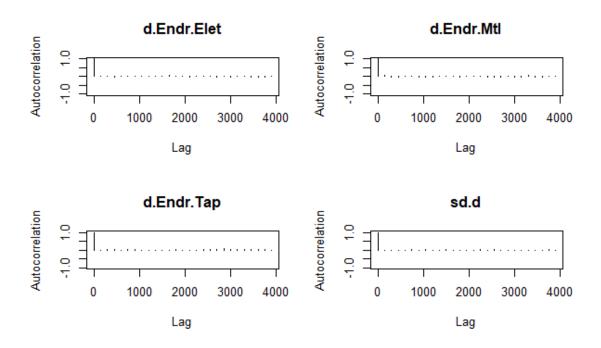
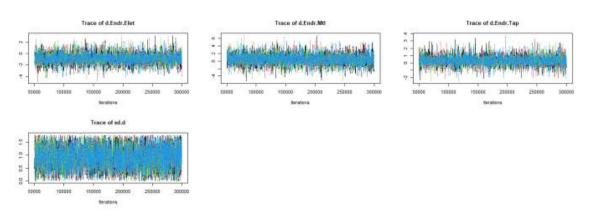


Figure S7. MCMC simulation for GR outcome



Traceplot



4. DISCUSSÃO

Essa tese apresentou dois estudos que levam em consideração desfechos (AG e RG) importantes, não somente para a estética, mas também para a qualidade de vida dos indivíduos (WAGNER et al., 2016). O primeiro, um estudo transversal que aborda os fatores associados com as AG, com estimativas e análise multinível de fatores associados em uma amostra representativa da área rural e o segundo estudo, é a primeira NMA realizada avaliando as características de escovas dentais que podem causar AG e RG.

A avaliação destes desfechos com estudos de diferentes delineamentos surgiram através de lacunas encontradas na literatura e pela necessidade de estudos com alto nível de evidencia sobre a associação entre Abrasões gengivais, recessões gengivais e hábitos de higiene. Estudos com uma metodologia como a NMA que fornece evidências comparativas para tratamentos não comparados diretamente em um ECR direto são necessários para sanar duvidas clínicas com uma evidência segura (CHAIMANI, 2022). Assim como, o desenho observacional transversal avalia a prevalência e fatores associados de uma condição entre uma população em geral com base em seu comportamento normal. Apesar das dificuldades de execução estes trabalhos mostram resultados, se bem executados metodologicamente, com um alto nível de evidência. (VAN DER WEIJDEN, 2011; ROSEMA et al., 2014).

Baseado nos resultados desta tese pode-se dizer que em uma população rural, a frequência de escovação maior que 2x ao dia e o tipo de cerdas de escova duras são associados a maiores extensões de AG. Alem disso, hipersensibilidade dentinária e recessão gengival também se apresentam associadas a AG. Também, indivíduos com maior índice de placa e gengivite apresentam menos AG. Assim como os resultados de nosso primeiro estudo, em nossa NMA as escovas manuais com cerdas macias apresentam-se seguras para AG. Já, os resultados da SUCRA indicaram um bom equilíbrio de escovas dentais manuais com filamentos arredondados presentes para ambos os desfechos, destacando essa característica da escova como a mais segura para evitar o desenvolvimento/progressão de GA e GR.

E necessário destacar que Abrasões gengivais possuem grande variabilidade, podendo esperar que estas AG superficiais cicatrizem naturalmente, diferente das RG, que são uma migração da margem gengival, apical à junção cemento-esmalte, resultando na superfície radicular exposição ROSEMA et al., 2014), sendo portanto, nosso desfecho principal mais relevante. Diante disso, com relação a magnitude do quanto essas comparações realizadas na NMA representam diferenças clinicamente importantes para RG, é importante destacar que não passam de 1mm. Não apresentando, portanto, diferenças com impacto clínico importante.

Apesar disso, nossos dados reforçam a recomendação da ADA, onde, as escovas de cerdas macias com pontas arredondadas parecem ser a melhor opção para AG e RG. E que escovas elétricas são tão seguras quanto as manuais macias. No entanto, outras características de higiene bucal parecem ser importantes. A atenção à frequência, duração, força e técnica de escovação também são fatores importantes que podem aumentar o risco de desenvolver recessão gengival (Rajapakse et al. 2007; Heasman et al. 2015). Além disso, o biótipo gengival fino (Cortellini & Bissada, 2018) e o nível socioeconômico também devem ser levados em consideração, o que remete à ideia de que o perfil e o comportamento do indivíduo também influenciam em nossos desfechos avaliados.

Em ambos os estudos, algumas limitações são encontradas e portanto, devem ser levadas em consideração como recomendações para futuros estudos. GA é uma condição dinâmica e pode refletir apenas a última escovação realizada. Para a coleta de dados, os participantes foram previamente agendados para o exame. Assim, podem ter realizado escovação traumática na tentativa de escovar "melhor" antes do exame clínico. No entanto, esse efeito Hawthorne é de difícil controle e está praticamente implícito em estudos com coleta de dados clínicos. Outra limitação é que não coletamos dados sobre o biótipo gengival devido às dificuldades na mensuração dessa variável. Em nossa NMA, poucos ECRs foram elegíveis, as redes são em forma de estrela e mal conectadas, dependendo em grande parte de comparações indiretas. Todas as comparações foram baixas ou muito baixas, certamente resultando em incertezas em torno das estimativas. Portanto, os resultados desta NMA devem ser interpretados com cautela.

A presente tese confirma que certos hábitos diários e dispositivos de higiene bucal estão associados à AG e RG. Esses resultados podem contribuir para o estabelecimento de estratégias de prevenção focadas na redução de desfechos importantes que exercem impacto negativo na qualidade de vida relacionada à saúde bucal, como a recessão gengival e a hipersensibilidade dentinária. Além disso, estudos envolvendo a investigação das condições de saúde bucal em moradores da zona rural são necessários devido ao acesso limitado dessa população ao atendimento médico e odontológico. Assim, os problemas e necessidades dessa população podem ser identificados para viabilizar o planejamento de políticas de saúde voltadas à universalidade e equidade, que são fatores que afetam a saúde bucal e têm consequências para a qualidade de vida.

5. CONSIDERAÇÕES FINAIS

Com base nas investigações científicas apresentadas nessa tese e conforme suas limitações, conclui-se que, em uma população rural do sul do Brasil a abrasão gengival apresenta-se independentemente associada à hipersensibilidade dentinária, recessão gengival, maior frequência de escovação e dureza das cerdas das escovas. E que escovas macias com filamentos arredondados é a melhor característica de escova de dentes a evitar tanto para GA quanto para GR.

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The aim of the *Journal of Clinical Periodontology* is to provide a platform for the exchange of scientific and clinical progress in the field of periodontology and allied disciplines, and to do so at the highest possible level. The Journal also aims to facilitate the application of new scientific knowledge to the daily practice of the concerned disciplines and addresses both practicing clinicians and members of the academic community.

The Journal is the official publication of the European Federation of Periodontology but serves an international audience by publishing contributions of high scientific merit in the fields of periodontology and implant dentistry. The journal accepts a broad spectrum of original work characterized as clinical or preclinical, basic or translational, as well as authoritative reviews, and proceedings of important scientific workshops. The journal's scope encompasses the physiology and pathology of the periodontal and peri-implant tissues, the biology and the modulation of periodontal and peri-implant tissue healing and regeneration, the diagnosis, etiology, epidemiology, prevention and therapy of periodontal and peri-implant diseases and conditions, the association of periodontal infection/inflammation and general health, and the clinical aspects of comprehensive rehabilitation of the periodontitis-affected patient.

3. MANUSCRIPT CATEGORIES AND REQUIREMENTS

Journal of Clinical Periodontology publishes original research articles, reviews, clinical innovation reports and case reports. The latter will be published only if they provide new fundamental knowledge and if they use language understandable to the clinician. It is expected that any manuscript submitted represents unpublished original research.

i. Original Research Articles

Original Research articles must describe significant and original experimental observations and provide sufficient detail so that the observations can be critically evaluated and, if necessary, repeated. Original articles will be published under the heading of clinical periodontology, implant dentistry or pre-clinical sciences and must conform to the highest international standards in the field.

Word limit: 3,500 words maximum, excluding references.

Abstract: 200 words maximum; must be structured, under the sub-headings: Aim(s), Materials and methods, Results, Conclusion(s).

Figures/Tables: Total of no more than 7 figures and tables.

Introduction: should be focused, outlining the historical or logical origins of the study and not summarize the results; exhaustive literature reviews are not appropriate. It should close with the explicit statement of the specific aims of the investigation.

Material and Methods: must contain sufficient detail such that, in combination with the references cited, all clinical trials and experiments reported can be fully reproduced. As a condition of publication, authors are required to make materials and methods used freely available to academic researchers for their own use. This includes antibodies and the constructs used to make transgenic animals, although not the animals themselves.

Results: should present the observations with minimal reference to earlier literature or to possible interpretations.

Discussion: may usefully start with a brief summary of the major findings, but repetition of parts of the abstract or of the results section should be avoided. The discussion section should end with a brief conclusion and a comment on the potential clinical relevance of the findings. Statements and interpretation of the data should be appropriately supported by original references.

The discussion may usefully be structured with the following points in mind (modified from the proposal by Richard Horton (2002), The Hidden Research Paper, The Journal of the American Medical Association, 287, 2775-2778). Not all points will apply to all studies and its use is optional, but we believe it will improve the discussion section to keep these points in mind.

Summary of key finding

- Primary outcome measure(s)
- Secondary outcome measure(s)
- Results as they relate to a prior hypothesis

Strengths and Limitations of the Study

- Study Question
- Study Design
- Data Collection
- Analysis
- Interpretation
- Possible effects of bias on outcomes

Interpretation and Implications in the Context of the Totality of Evidence

- Is there a systematic review to refer to?
- If not, could one be reasonably done here and now?
- What this study adds to the available evidence
- Effects on patient care and health policy
- Possible mechanisms

Controversies Raised by This Study Future Research Directions

- For this particular research collaboration
- Underlying mechanisms
- Clinical research

ii. Clinical Innovation Reports

Clinical Innovation Reports are suited to describe significant improvements in clinical practice such as the report of a novel surgical technique, a breakthrough in technology or practical approaches to recognized clinical challenges. They should conform to the highest scientific and clinical practice standards.

Word limit: 3,000 words maximum, excluding references.

Main text: should be organized with Introduction; Clinical Innovation Report; Discussion and Conclusion.

Figures/Tables: Total of no more than 12 figures and tables.

iii. Case Reports

Case Reports illustrating unusual and clinically relevant observations are acceptable, but their merit needs to provide high priority for publication in the Journal. On rare occasions, completed cases displaying non-obvious solutions to significant clinical challenges will be considered.

Main text: should be organised with Introduction; Case report; Discussion and Conclusion.

iv. Reviews and Systematic Reviews

The Journal primarily publishes invited reviews or systematic reviews by experts in the field.

Unsolicited systematic reviews may be considered under the following conditions:

- 1. In the submission letter, the authors convincingly articulate the novelty of the findings, and the potential impact of the review on clinical practice, policy or research.
- There is enough new evidence generated by high quality/large sample size studies that has the potential to modify the conclusions supported by systematic reviews published to date.
- If not a Cochrane review, the systematic review has been prospectively registered in PROSPERO (https://www.crd.york.ac.uk/prospero/).

Word limit: 4,000 words maximum, excluding references.

Main text: should be organized with Introduction; Review; Discussion and Conclusion.

Revisions and Resubmissions

Please note that all revisions and resubmissions of papers should also include a separate rebuttal and a tracked changes document to assist in peer review.

4. PREPARING THE SUBMISSION

Free Format submission

Journal of Clinical Periodontology now offers Free Format submission for a simplified and streamlined submission process. Before you submit, you will need:

- Your manuscript: this can be a single file including text, figures, and tables, or separate files whichever you prefer. All required sections should be contained in your manuscript, including a title page with all author details, including affiliations and email addresses, a statement of clinical relevance, abstract, introduction, methods, results, and conclusions. Figures and tables should have legends. References may be submitted in any style or format, as long as it is consistent throughout the manuscript. If the manuscript, figures or tables are difficult for you to read, they will also be difficult for the editors and reviewers. If your manuscript is difficult to read, the editorial office may send it back to you for revision.
 - (Why is this important? We need to make sure your manuscript is suitable for review.)
- Statements relating to our ethics and integrity policies:
 - Conflict of interest disclosure
 - O Statement of funding source
 - o Ethical approval statement
 - O Patient consent statement (if appropriate)
 - o permission to reproduce material from other sources
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 (Why is this important? We need to uphold rigorous ethical standards for the research we consider for publication.)
- Your co-author details, including affiliation and email address. (Why is this important? We need to keep all co-authors informed of the outcome of the peer review process.)
- An ORCID ID, freely available at https://orcid.org. (Why is this important? Your article, if accepted and published, will be attached to your ORCID profile. Institutions and funders are increasingly requiring authors to have ORCID IDs.)

To submit, login at https://mc.manuscriptcentral.com/jcpe and create a new submission. Follow the submission steps as required and submit the manuscript.

If you are invited to revise your manuscript after peer review, the journal will also request the revised manuscript to be formatted according to journal requirements as described below.

Cover Letters

A cover letter is mandatory and must be signed by the corresponding author. It is required to confirm that the submitted work is (i) original, (ii) not currently under consideration for publication elsewhere, and (iii) in compliance with all rules stipulated by the Journal.

Parts of the Manuscript

Manuscripts can be uploaded either as a single document (containing the main text, tables and figures), or with figures and tables provided as separate files. Should your manuscript reach revision stage, figures and tables must be provided as separate files. The main manuscript file can be submitted in Microsoft Word (.doc or .docx) format.

Main Text File

Your main document file should include:

- i. A short informative title containing the major key words. The title should not contain abbreviations;
- ii. The full names of the authors with institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
- iii. Acknowledgments;
- iv. Abstract structured (intro/methods/results/conclusion) or unstructured;
- v. Up to seven keywords;
- vi. Main body: formatted as introduction, materials & methods, results, discussion, conclusion
- vii. References
- viii. Tables (each table complete with title and footnotes);
- ix. Figures: Figure legends must be added beneath each individual image during upload AND as a complete list in the text:
- x. Appendices (if relevant)

Figures and supporting information should be supplied as separate files.

Authorship

Please refer to the journal's authorship policy the Editorial Policies and Ethical Considerations section for details on eligibility for author listing.

Acknowledgments

Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.

Conflict of Interest Statement

Authors will be asked to provide a conflict of interest statement during the submission process. For details on what to include in this section, see the section 'Conflict of Interest' in the Editorial Policies and Ethical Considerations section below. Submitting authors should ensure they liaise with all co-authors to confirm agreement with the final statement.

Abstract

The abstract is limited to 200 words in length and should not contain abbreviations or references. The abstract should be organized according to the content of the paper.

For Original Research Articles the abstract should be organized with aim, materials and methods, results and conclusions.

For clinical trials, it is encouraged that the abstract finish with the clinical trial registration number on a free public database such as clinicaltrials.gov.

Keywords

Please provide 1-5 keywords. When appropriate keywords are available, they should be taken from those recommended by the US National Library of Medicine's Medical Subject Headings (MeSH) browser list at www.nlm.nih.gov/mesh. Authors may add specific keywords.

Main Text

All manuscripts should emphasize clarity and brevity. Authors should pay special attention to the presentation of their findings so that they may be communicated clearly. Technical jargon should be avoided as much as possible and be clearly explained where its use is unavoidable.

Clinical Relevance

This section is aimed at giving clinicians a reading light to put the present research in perspective. It should be no more than 100 words and should not be a repetition of the abstract. It should provide a clear and concise explanation of the rationale for the study, of what was known before and of how the present results advance knowledge of this field. If appropriate, it may also contain suggestions for clinical practice.

It should be structured with the following headings: Scientific rationale for study; Principal findings; Practical implications.

Authors should pay particular attention to this text as it will be published in a highlighted box within their manuscript; ideally, reading this section should leave clinicians wishing to learn more about the topic and encourage them to read the full article

References

It is the policy of the Journal to encourage reference to the original papers rather than to literature reviews. Authors should therefore keep citations of reviews to the absolute minimum.

References should be prepared according to the Publication Manual of the American Psychological Association (6th edition). This means in text citations should follow the author-date method whereby the author's last name and the year of publication for the source should appear in the text, for example, (Jones, 1998). The complete reference list should appear alphabetically by name at the end of the paper.

A sample of the most common entries in reference lists appears below. Please note that a DOI should be provided for all references where available. For more information about APA referencing style, please refer to the APA FAQ. Please note that for journal articles, issue numbers are not included unless each issue in the volume begins with page one.

Journal article

Beers, S. R., & De Bellis, M. D. (2002). Neuropsychological function in children with maltreatment-related posttraumatic stress disorder. The American Journal of Psychiatry, 159, 483–486. doi:10.1176/appi.ajp.159.3.483

Rook

Bradley-Johnson, S. (1994). Psychoeducational assessment of students who are visually impaired or blind: Infancy through high school (2nd ed.). Austin, TX: Pro-ed.

Chapter in an Edited Book

Borstrøm, I., & Elbro, C. (1997). Prevention of dyslexia in kindergarten: Effects of phoneme awareness training with children of dyslexic parents. In C. Hulme & M. Snowling (Eds.), Dyslexia: Biology, cognition and intervention (pp. 235–253). London: Whurr.

Internet Document

Norton, R. (2006, November 4). How to train a cat to operate a light switch [Video file]. Retrieved from http://www.youtube.com/watch?v=Vja83KLQXZ

Please note that all unpublished papers (submitted or in press) included in the reference list should be provided in a digital version at submission. The unpublished paper should be uploaded as a supplementary file for review.

Tables

Tables should be self-contained and complement, not duplicate, information contained in the text. They should be supplied as editable files, not pasted as images. Legends should be concise but comprehensive – the table, legend, and footnotes must be understandable without reference to the text. All abbreviations must be defined in footnotes. Footnote symbols: \dagger , \ddagger , \$, \P , should be used (in that order) and *, **, *** should be reserved for P-values. Statistical measures such as SD or SEM should be identified in the headings.

Figure Legends

Legends should be concise but comprehensive – the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement.

Figures

Although authors are encouraged to send the highest-quality figures possible, for peer-review purposes, a wide variety of formats, sizes, and resolutions are accepted.

for the basic figure requirements for figures submitted with manuscripts for initial peer review, as well as the more detailed post-acceptance figure requirements.

Colour Figures. Figures submitted in colour may be reproduced in colour online free of charge. Please note, however, that it is preferable that line figures (e.g. graphs and charts) are supplied in black and white so that they are legible if printed by a reader in black and white.

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Additional Files

Appendices

Appendices will be published after the references. For submission they should be supplied as separate files but referred to in the text.

Supporting Information

Supporting information is information that is not essential to the article, but provides greater depth and background. It is hosted online and appears without editing or typesetting. It may include tables, figures, videos, datasets, etc.

Wiley's FAQs on supporting information.

Note: if data, scripts, or other artefacts used to generate the analyses presented in the paper are available via a publicly available data repository, authors should include a reference to the location of the material within their paper.

General Style Points

The following points provide general advice on formatting and style.

Abbreviations, Symbols and Nomenclature: Journal of Clinical Periodontology adheres to the conventions
outlined in Units, Symbols and Abbreviations: A Guide for Medical and Scientific Editors and Authors.
Abbreviations should be kept to a minimum, particularly those that are not standard. Non-standard abbreviations
must be used three or more times and written out completely in the text when first used.

Resource Identification Initiative

The journal supports the Resource Identification Initiative, which aims to promote research resource identification, discovery, and reuse. This initiative, led by the Neuroscience Information Framework and the Oregon Health & Science University Library, provides unique identifiers for antibodies, model organisms, cell lines, and tools including software and databases. These IDs, called Research Resource Identifiers (RRIDs), are machine-readable and can be used to search for all papers where a particular resource was used and to increase access to critical data to help researchers identify suitable reagents and tools.

Authors are asked to use RRIDs to cite the resources used in their research where applicable in the text, similar to a regular citation or Genbank Accession number. For antibodies, authors should include in the citation the vendor, catalogue number, and RRID both in the text upon first mention in the Methods section. For software tools and databases, please provide the name of the resource followed by the resource website, if available, and the RRID. For model organisms, the RRID alone is sufficient

Additionally, authors must include the RRIDs in the list of keywords associated with the manuscript.

To Obtain Research Resource Identifiers (RRIDs)

- 1. Use the Resource Identification Portal, created by the Resource Identification Initiative Working Group.
- 2. Search for the research resource (please see the section titled "Search Features and Tips" for more information).
- 3. Click on the "Cite This" button to obtain the citation and insert the citation into the manuscript text.

If there is a resource that is not found within the Resource Identification Portal, authors are asked to register the resource with the appropriate resource authority. Information on how to do this is provided in the "Resource Citation Guidelines" section of the Portal.

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Manuscript Preparation Tips: Wiley has a range of resources for authors preparing manuscripts for submission

available here. In particular, authors may benefit from referring to Wiley's best practice tips on Writing for Search Engine Optimization.

Article Preparation Support: Wiley Editing Services offers expert help with English Language Editing, as well as translation, manuscript formatting, figure illustration, figure formatting, and graphical abstract design – so you can submit your manuscript with confidence.

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Japanese authors can also find a list of local English improvement services

at http://www.wiley.co.jp/journals/editcontribute.html All services are paid for and arranged by the author, and use of one of these services does not guarantee acceptance or preference for publication.

Guidelines for Cover Submission

If you would like to send suggestions for artwork related to your manuscript to be considered to appear on the cover of the journal, please follow these guidelines

5. EDITORIAL POLICIES AND ETHICAL CONSIDERATIONS

Peer Review and Acceptance

The acceptance criteria for all papers are the quality and originality of the research and its significance to journal readership. Manuscripts are single-blind peer reviewed. Papers will only be sent to review if the Editor-in-Chief determines that the paper meets the appropriate quality and relevance requirements.

Wiley's policy on the confidentiality of the review process is available here.

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Under exceptional circumstances, authors may appeal the editorial decision. Authors who wish to appeal the decision on their submitted paper may do so by e-mailing the editorial office at cpeedoffice@wiley.com with a detailed explanation for why they find reasons to appeal the decision.

Human Studies and Subjects

For manuscripts reporting medical studies that involve human participants, a statement identifying the ethics committee that approved the study and confirmation that the study conforms to recognized standards is required, for example: Declaration of Helsinki; US Federal Policy for the Protection of Human Subjects; or European Medicines Agency Guidelines for Good Clinical Practice. It should also state clearly in the text that all persons gave their informed consent prior to their inclusion in the study.

Patient anonymity should be preserved. When detailed descriptions, photographs, or videos of faces or identifiable body parts are used that may allow identification, authors should obtain the individual's free prior informed consent. Authors do not need to provide a copy of the consent form to the publisher; however, in signing the author license to publish, authors are required to confirm that consent has been obtained. Wiley has a standard patient consent form available for use. Where photographs are used they need to be cropped sufficiently to prevent human subjects being recognized; black eye bars should not be used as they do not sufficiently protect an individual's identity).

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A statement indicating that the protocol and procedures employed were ethically reviewed and approved, as well as the name of the body giving approval, must be included in the Methods section of the manuscript. Authors are encouraged to adhere to animal research reporting standards, for example the ARRIVE guidelines for reporting study design and statistical analysis; experimental procedures; experimental animals and housing and husbandry. Authors should also state whether experiments were performed in accordance with relevant institutional and national guidelines for the care and use of laboratory animals:

- US authors should cite compliance with the US National Research Council's Guide for the Care and Use of Laboratory Animals, the US Public Health Service's Policy on Humane Care and Use of Laboratory Animals, and Guide for the Care and Use of Laboratory Animals.
- UK authors should conform to UK legislation under the Animals (Scientific Procedures) Act 1986 Amendment Regulations (SI 2012/3039).
- European authors outside the UK should conform to Directive 2010/63/EU.

Clinical Trial Registration

The Journal will only consider for publication clinical trials that have been registered *prospectively* in a publicly accessible database. (Please note that the International Committee of Medical Journal Editors require registration of clinical trials prior

to enrollment of the first participant. Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) states that Clinical Trials need to be registered within 21 days of enrollment of the first participant).

Studies that do not meet the above requirements for potentially valid reasons (e.g., manuscripts reporting on long-term outcomes of trials initiated in the distant past) may be considered after special deliberation among the Associate Editors and the Editor in Chief.

The registration database, the registration number, and the registration date must be noted at the end of the abstract as well as in the text of the Materials and Methods.

Research Reporting Guidelines

Accurate and complete reporting enables readers to fully appraise research, replicate it, and use it. Authors are required to adhere to recognised research reporting standards. The EQUATOR Network collects more than 370 reporting guidelines for many study types, including for:

· Randomised trials: CONSORT

Clinical trials should be reported using the CONSORT guidelines. A CONSORT checklist should also be included in the submission material. If your study is a randomized clinical trial, you will need to fill in all sections of the CONSORT Checklist. If your study is not a randomized trial, not all sections of the checklist might apply to your manuscript, in which case you simply fill in N/A.

Observational studies : STROBESystematic reviews : PRISMA

• Case reports : CARE

• Qualitative research : SRQR

Diagnostic / prognostic studies : STARD
 Quality improvement studies : SQUIRE
 Economic evaluations : CHEERS
 Animal pre-clinical studies : ARRIVE

Study protocols : SPIRIT

• Clinical practice guidelines : AGREE

We also encourage authors to refer to and follow guidelines from:

- Future of Research Communications and e-Scholarship (FORCE11)
- National Research Council's Institute for Laboratory Animal Research guidelines
- The Gold Standard Publication Checklist from Hooijmans and colleagues
- Minimum Information Guidelines from Diverse Bioscience Communities (MIBBI) website
- FAIRsharing website

Species Names

Upon its first use in the title, abstract, and text, the common name of a species should be followed by the scientific name (genus, species, and authority) in parentheses. For well-known species, however, scientific names may be omitted from article titles. If no common name exists in English, only the scientific name should be used.

Genetic Nomenclature

Sequence variants should be described in the text and tables using both DNA and protein designations whenever appropriate. Sequence variant nomenclature must follow the current HGVS guidelines; see varnomen.hgvs.org, where examples of acceptable nomenclature are provided.

Sequence Data

Nucleotide sequence data can be submitted in electronic form to any of the three major collaborative databases: DDBJ, EMBL, or GenBank. It is only necessary to submit to one database as data are exchanged between DDBJ, EMBL, and GenBank on a daily basis. The suggested wording for referring to accession-number information is: 'These sequence data have been submitted to the DDBJ/EMBL/GenBank databases under accession number U12345'. Addresses are as follows:

- DNA Data Bank of Japan (DDBJ): www.ddbj.nig.ac.jp
- EMBL Nucleotide Archive: ebi.ac.uk/ena

GenBank: <u>www.ncbi.nlm.nih.gov/genbank</u>

Proteins sequence data should be submitted to either of the following repositories:

• Protein Information Resource (PIR): pir.georgetown.edu

• SWISS-PROT: expasy.ch/sprot/sprot-top

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For papers describing structural data, atomic coordinates and the associated experimental data should be deposited in the appropriate databank (see below). Please note that the data in databanks must be released, at the latest, upon publication of the article. We trust in the cooperation of our authors to ensure that atomic coordinates and experimental data are released on time.

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- Inorganic compounds: Fachinformationszentrum Karlsruhe (FIZ; fiz-karlsruhe.de).
- Proteins and nucleic acids: *Protein Data Bank* (<u>rcsb.org/pdb</u>).
- NMR spectroscopy data: *BioMagResBank* (bmrb.wisc.edu).

Conflict of Interest

The journal requires that all authors disclose any potential sources of conflict of interest. Any interest or relationship, financial or otherwise that might be perceived as influencing an author's objectivity is considered a potential source of conflict of interest. These must be disclosed when directly relevant or directly related to the work that the authors describe in their manuscript. Potential sources of conflict of interest include, but are not limited to: patent or stock ownership, membership of a company board of directors, membership of an advisory board or committee for a company, and consultancy for or receipt of speaker's fees from a company. The existence of a conflict of interest does not preclude publication. If the authors have no conflict of interest to declare, they must also state this at submission. It is the responsibility of the corresponding author to review this policy with all authors and collectively to disclose with the submission ALL pertinent commercial and other relationships. Please provide adequate detail that allows reproduction of the analyses after access to the original data. Be explicit about the basis of computation of the sample size and the power calculations. For clinical trials, Intent-to-treat analyses are expected, and may be supplemented by per-protocol or other types of analyses, if applicable.

See former Editor-in-Chief Maurizio Tonetti's Editorial on Conflict of Interest and Source of Funding and www.icmje.org/#conflicts for generally accepted definitions.

The above policies are in accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals produced by the International Committee of Medical Journal Editors (http://www.icmje.org/). It is the responsibility of the corresponding author to have all authors of a manuscript fill out a conflict of interest disclosure form, and to upload all forms together with the manuscript on submission. The disclosure statement should be included under Acknowledgements. Please find the form below:

Conflict of Interest Disclosure Form

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Authors should list all funding sources at submission. Authors are responsible for the accuracy of their funder designation. If in doubt, please check the Open Funder Registry for the correct nomenclature: https://www.crossref.org/services/funder-registry/

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- 3. Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Journal of Clinical Periodontology expects that data supporting the results in the paper will be archived in an appropriate public repository. Authors are required to provide a data availability statement to describe the availability or the absence of shared data. When data have been shared, authors are required to include in their data availability statement a link to the repository they have used, and to cite the data they have shared. Whenever possible the scripts and other artefacts used to generate the analyses presented in the paper should also be publicly archived. If sharing data compromises ethical standards or legal requirements then authors are not expected to share it.

See the Standard Templates for Author Use to select an appropriate data availability statement for your dataset.

Human subject information in databases. The journal refers to the World Health Medical Association Declaration of Taipei on Ethical Considerations Regarding Health Databases and Biobanks

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Accepted article received in production

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and proofed articles will appear in an issue on Wiley Online Library; the link to the article in PubMed will update automatically.

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8. POST PUBLICATION

Access and sharing

When the article is published online:

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- The link to the published article can be shared through social media.
- The author will have free access to the paper (after accepting the Terms & Conditions of use, they can view the article).
- The corresponding author and co-authors can nominate up to ten colleagues to receive a publication alert and free online access to the article.

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9. EDITORIAL OFFICE CONTACT DETAILS

For queries about submissions, please contact cpeedoffic