

SYSTEMATIC REVIEW

Scientific evidence on the efficacy of effervescent tablets for cleaning removable prostheses. A systematic review and meta-analysis

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ABSTRACT

Statement of problem. Scientific evidence to determine the optimal method of cleaning and disinfecting removable prostheses is lacking.

Purpose. The purpose of this systematic review and meta-analysis was to evaluate the effectiveness of effervescent tablets in the cleaning and sanitizing of removable prostheses compared with other chemical and physical methods by assessing the reduction of biofilm, microbial levels, and material stability.

Material and methods. A systematic literature search and meta-analysis was conducted in August 2021 in the MEDLINE/PubMed, Cochrane, Embase, Scopus, and Web of Science databases. Randomized and nonrandomized controlled clinical trials published in English were included without publication year limits. A total of 23 studies were included in the systematic review and 6 in the meta-analysis, which had been registered in the international prospective register of systematic reviews (PROSPERO) database (CRD42021274019). The Cochrane Collaboration tool was used to assess the risk of bias of randomized clinical trials. The physiotherapy evidence database (PEDro) scale was used to analyze the internal validity of clinical trials by assessing the quality of the data obtained. The studies included in the meta-analysis were combined by using a random-effects model with the inverse variance method. Publication bias was analyzed by using the Duval and Tweedie trim-and-fill method.

Results. With regard to biofilm reduction, the standardized mean difference estimated with the 4 studies combined in the meta-analysis was $P=.012$: mean difference=-1.92; 95% confidence interval=-3.45 to -0.38, indicating a “large” effect of the combination of brushing and effervescent tablet versus brushing alone. To estimate the reduction in the total bacteria levels in the 3 combined studies, a “large” effect size was obtained for the combination of brushing and using an effervescent tablet versus brushing alone, $P<.001$: mean difference=-4.43; 95% confidence interval=-8.29 to -0.55. Finally, when the 3 studies were combined to assess the reduction of *Candida* or fungal infection, a “moderate” effect size was obtained for the combination of brushing combined with the use of an effervescent tablet, $P<.001$: mean difference=-0.78; 95% confidence interval=-1.19 to -0.37.

Conclusions. The combination of brushing and the use of effervescent tablets versus brushing alone had a significantly higher effect on reducing biofilm and bacterial counts and a moderate effect on reducing *Candida*. Regarding color and dimensional stability, few studies were found, with the results depending on the concentration of the product and the immersion time of the device. (J Prosthet Dent 2023;■:■-■)

Hygiene and the disinfection of removable prostheses is essential to remove biofilm, increase longevity, and maintain good oral health.¹ Stomatitis has been reported to be the main cause of superinfection in patients with

prostheses, especially infection with *Candida* spp.² Poor denture hygiene has not only been associated with problems in the oral cavity but also with a 2.4 times higher risk of severe pneumonia.³

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Clinical Implications

Evidence that one chemical method is better than another is lacking. Strong evidence was found that the use of effervescent tablets in conjunction with brushing has a significant effect on the reduction of biofilm and microbial levels when compared with brushing alone.

The ideal hygiene product or system would achieve an optimal level of disinfection of the dentures, be nontoxic, and avoid alterations in the physical and mechanical properties, such as color and dimension. In addition, it should be affordable.⁴ Among the mechanical methods for cleaning dentures, brushing is the most used because of its simplicity, effectiveness, and low cost.⁴⁻⁶

The combination of brushing with nonabrasive toothpaste⁷ together with a chemical method consisting of immersing the prosthesis in disinfectant solutions such as alkaline peroxide effervescent tablets, lauryl sulfate solutions, 0.5% sodium hypochlorite (NaOCl), or even 0.2% chlorhexidine digluconate significantly reduces the level of microorganism colony-forming units (CFUs) compared with brushing with water alone.^{6,8}

Effervescent tablets based on alkaline peroxides provide a straightforward chemical method which does not require dosing. Efficacy has been attributed to the mechanical action produced by the effervescence generated when the peroxide dissolves in water, with the additional benefit that the resulting solution generates oxygen free radicals that have an antimicrobial action and enzymes that break down biofilm proteins.^{9,10} These products appear to be effective against *Streptococcus mutans* because of their superficial location on the biofilm.¹¹ Furthermore, the resistance of *Candida* to disinfection methods has been associated with the thickness of the cell wall, formed by peptidoglycans.¹² Therefore, other methods such as ultrasonic cleaning together with tablets have been recommended to reduce the number of more resistant species and could be indicated for denture sanitizing in institutionalized or elderly patients with an increased prevalence of *Candida*.^{11,13-15} Physical methods, such as microwave irradiation and photodynamic therapy, could also be used to complement these mechanical and chemical methods.⁶

Two systematic reviews^{6,16} and 1 meta-analysis carried out by the Cochrane Library based on a single article¹⁷ evaluated the efficacy of the use of tablets in sanitizing removable prostheses and in assessing the reduction of biofilm, change in color, and dimensional alteration. The studies concluded that quality evidence is lacking because of the heterogeneity of the methodology used. They all concluded that the combination of

mechanical and chemical methods achieved higher levels of sanitizing and disinfection in removable prostheses.

The aim of the present study was to provide an updated systematic review and meta-analysis on the efficacy of using denture cleaning tablets with or without brushing, compared with other cleaning methods, by assessing biofilm reduction, microbial levels, and the stability of materials. The null hypothesis was that the use of effervescent tablets alone or combined with brushing would not be more effective than other methods of cleaning removable prostheses.

MATERIAL AND METHODS

This systematic review was conducted following the guidelines of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 statement.¹⁸ The protocol for this systematic review was registered in the international prospective register of systematic reviews (PROSPERO) under the reference number: CRD42021274019.

Randomized and nonrandomized controlled clinical trials were included in the systematic review, and no limits were set on the year of publication. Table 1 describes the study question posed according to the population, intervention, comparison, outcome (PICO) framework with the inclusion and exclusion criteria of the articles, the databases used, and the search strategy. The search was conducted in August 2021.

The resulting articles were divided into 2 groups to select those eligible after reading the title and abstract. Two researchers (J.M.M., V.A.) reviewed half the articles and the other 2 (Y.M., C.L.L.) the other half. The articles selected in this phase were again divided into 2 groups and the full text evaluated. Articles that met the inclusion criteria were selected for data extraction. At all stages, in the event of disagreement between a pair of researchers, the items were evaluated by the other pair. The concordance between the pairs of reviewers was analyzed by using the Cohen kappa coefficient.

The efficacy of the use of effervescent tablets alone or in combination was analyzed against other methods and combinations of mechanical or chemical cleaning or against a control. The variables recorded were percentage reduction in the amount of biofilm on the denture surface or visible plaque score, changes in the number of CFUs of microorganisms, changes in microbial composition, and changes in dimensional stability or color. Wherever possible, quantitative data were included for each of the study outcomes by noting percentages and the means and standard deviations of quantitative variables.

The risk of bias and quality assessment of the selected studies with the Cochrane Collaboration tool¹⁹ was also performed by pairs of researchers. The Physiotherapy

Table 1. Strategy used in systematic search

| | |
|------------------------------------|--|
| Population (P) | Patients with complete or partial removable dentures, removable orthodontic appliances, retainers, or occlusal splints. |
| Intervention (I) | Use of effervescent tablets combined with brushing. |
| Comparison (C) | Other methods of cleaning the prosthesis: brushing, immersion in water or saline, immersion in hypochlorite, chlorhexidine or other cleaning products. |
| Outcome (O) | Cleaning efficiency: Reduction in the amount of biofilm or plaque, reduction or elimination of the number of colony-forming units (CFU) of microorganisms or changes in bacterial composition. Color stability. Dimensional stability. |
| PICO questions | <ul style="list-style-type: none"> • In patients wearing removable dentures (P) does use of effervescent tablets combined with brushing (I) provides superior sanitation (O) compared with brushing/effervescent tablets use alone (C)? • In patients wearing removable dentures (P) does use of effervescent tablets alone or combined with brushing (I) provides superior sanitation (O) compared with ultrasound vibration (C)? • In patients wearing removable dentures (P) does use of effervescent tablets alone or combined with brushing (I) provides superior sanitation (O) compared with immersion in water or saline, immersion in hypochlorite, chlorhexidine (C)? |
| Search terms | ((full dentures) OR (complete dentures) OR (removable prosthodontics) OR (partial dentures) OR (dentures) OR (removable dentures) OR (acrylic dentures) OR (overdentures) OR ("removable orthodontic appliances") OR ("Aligners") OR (orthodontic retainers) OR (thermoplastic retainers) OR ("occlusal splint") OR (denture wearers) OR (appliance wearers)) AND ((disinfect*) OR (disinfection agents) OR (cleansing agents) OR (chemical denture cleansers) OR (denture cleanser) OR (denture cleaning method) OR (cleansers) OR ("denture cleansing tablets") OR (alkaline peroxide tablets) OR (peroxide-based cleanser solution) OR (immersion) OR (overnight storage) OR ("effervescent tablets") OR ("ultrasonic devices") OR (brushing) OR (toothbrushing) OR (denture dentifrice) OR (microwave exposure) OR (soaking) OR (Hygiene) OR (Hygiene habits) OR (denture Hygiene)) AND ((effectiveness) OR (efficacy) OR (sanitation) OR (biofilm) OR ("denture biofilm") OR (antimicrobial effect) OR (microorganisms) OR (microbial) OR (denture cleanliness) OR (bacteria) OR (gram positive bacteria) OR (anaerobes) OR ("color stability") OR ("dimensional stability") OR (<i>Candida</i>) OR (bioluminescence) OR ("dimensional changes")) |
| Databases accessed electronically | MEDLINE/PubMed, Scopus, Cochrane, WOS, Embase. |
| Inclusion criteria | Randomized and nonrandomized controlled clinical trials. Use of effervescent tablets in at least one of the comparison groups. Amount of biofilm, bacterial levels and color or dimensional stability. |
| Exclusion criteria | Language other than English. Participants with stomatitis. Groups of less than 10 participants. Do not include the composition of the tablet or the trade name. |
| Exclusion criteria for publication | Selected articles carried out on patients with removable orthodontic appliances, retainers, or occlusal splints. |

Evidence Database (PEDro) scale was used to analyze the internal validity of the clinical trials.²⁰

The studies included in the meta-analysis were combined by using a random-effects model with the inverse variance method. Heterogeneity was considered when the *P* value of the *Q* test was less than .1 and/or when the value of the *I*² parameter was greater than 50%. In the absence of heterogeneity, the studies were pooled by default with a fixed effects model. The effect size measure used was the standardized mean difference, as it allows the combination of mean differences obtained on different scales and enables effect size to be classified according to Cohen as follows: "small" when the estimated difference is between 0.2 to 0.3; "medium or moderate" around 0.5 to 0.8; and "large" above 0.8.

Publication bias was analyzed by using the Duval and Tweedie²¹ trim-and-fill method, which assesses the change in the parameter estimate that occurs if any studies are added to improve the symmetry of the funnel plot. Also, the linear regression method intercept was assessed, which considers that bias is present if its 95% confidence interval does not include 0 and its 2-sided test

P value <.1. In the case of a significant estimate, the calculation of the number of nonsignificant studies required, known as the classic fail-safe number, was added so that the estimate was no longer significant. A software program (Comprehensive Meta-analysis, version 3.0; BioStat Inc) was used for the analysis. The grading of recommendations, assessment, development, and evaluation system (GRADE) scale was used²² in the search for the best available evidence.

RESULTS

Figure 1 illustrates the sequence in the selection of the articles that were included in the present review (23 articles) and those included in the meta-analysis (6 articles). Table 2 shows all the articles included and the data extracted from each of them. Supplemental Table 1 (available online), lists those excluded and the reason for exclusion. The concordance between the pairs of reviewers selecting the articles was high (JMM and VA kappa=0.81/YM and CLL kappa=0.83).

The included studies were published between 1984 and 2021. All studies were 2 to 6 arm randomized controlled

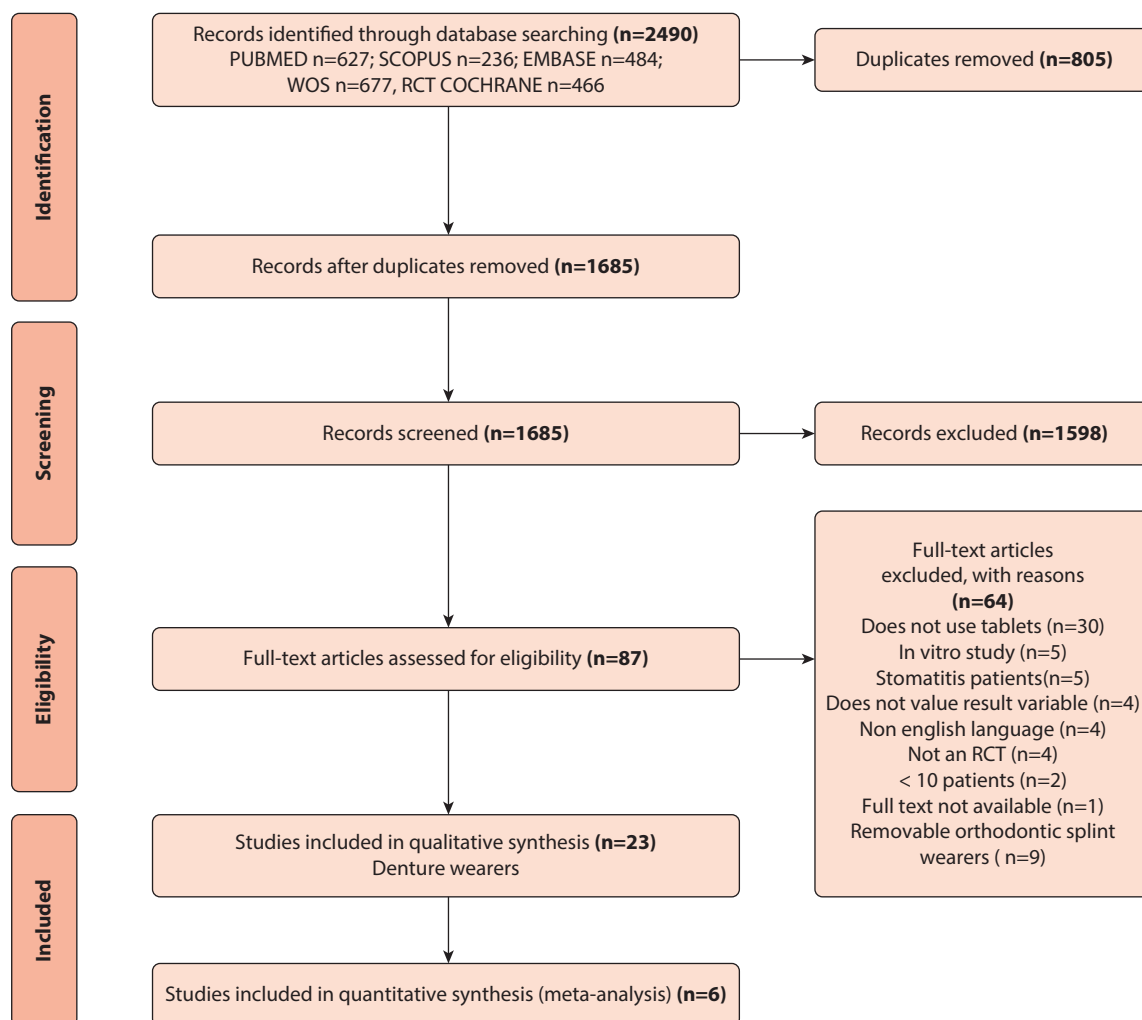


Figure 1. PRISMA diagram. PRISMA, preferred reporting items for systematic reviews and meta-analyses.

clinical trials; (RCTs), of which, 12 studies presented crossover designs with washout period and 1 of which used a split-mouth design. Participants age ranged from 43 to 101 years, and the number of participants per study ranged from 10 to 113. Comparisons between cleaning methods mainly combined brushing and the use of tablets of different brands and compositions (Supplemental Table 2, available online). These methods were also compared with immersions in 0.2% or 2% chlorhexidine digluconate or 0.5% NaOCl solutions. In addition, some studies added ultrasonic cleaning of the dentures. Eleven studies^{8,13,15,25,28,29,33,34,37,38,40} examined the effect of tablets versus other options on the amount of biofilm. In 11 other studies,^{11,14,15,24,28,31,36,39} the number of microorganisms was assessed. The presence of *Candida* was analyzed in 11 studies.^{8,11,14,15,25,28,32,35,38} Variation in color^{30,35} and roughness were analyzed in 2 studies,^{31,35} and only 1 study²³ analyzed dimensional stability.

The intrastudy risk of bias assessment is shown in Figure 2. The risk of bias for each study is presented in Figure 3. The internal validity and methodological quality are shown in Table 3 and Figure 4.

Some studies had shown better results in terms of *S. mutans* and biofilm reduction with only a nightly immersion in cleaning tablets (Corega, Denture Brite, Polident, Efferdent, and Bonyplus) versus single brushing of the prosthesis^{24,26} or versus immersion in water alone.^{15,27,28,33} Only 2 studies^{33,40} reported that brushing alone with specific pastes was more effective in reducing biofilm than the alkaline peroxide tablet alone (Efferdent, Polident, and Bonyplus). In general, most studies concluded that the combination of mechanical methods such as brushing with water, cleaning/toothpaste or neutral soap together with a chemical method with effervescent tablets reduced biofilm and bacteria.^{8,11,13-15,24-26,29,31,33,36-38} The results were not as

Table 2. Characteristics of studies (n=23) of complete denture wearers included in systematic review

| Study (Author/Year) | Type | Age (y) | Duration | Groups | Variables | Conclusions |
|-------------------------------|---------------|--|-----------|---|--|---|
| Baba 2018 ⁸ | RCT | GC \bar{x} :77.5 DS: \pm 7.92 GE \bar{x} :81.2 DS: \pm 4.79 | 21 d | 30 complete denture wearers. 2 groups: <ul style="list-style-type: none"> GC (n =15): Brushing for 2 min after each meal+soaking in saline overnight. GE (n=15): Brushing for 2 min after each meal+immersion in Polident tablet overnight. | <ul style="list-style-type: none"> Presence of luciferase by luminescence to measure cleanliness. <i>Candida albicans</i> count in the denture. Satisfaction and oral quality of life. | <p>Significant differences between 2 methods in luminescence and <i>Candida</i> count.</p> <p>Combination of brushing and Polident more effective than mechanical cleaning alone, No difference in patient satisfaction or oral quality of life between 2 methods</p> |
| Bouattour 2021 ²³ | Crossover RCT | \bar{x} :76.5 DS: \pm 5.9 | 21 d | 10 complete denture wearers. 2 groups: <ul style="list-style-type: none"> G1 (n=10): Overnight dry storage. G2 (n=10): Immersion in Kukident tablet overnight. | <ul style="list-style-type: none"> Dimensional stability measured with 3D Scanner, Iscan D103i. Posterior and vertical retention measured with dynamometer. | Although results slightly better in dry state, no significant changes in dimensional stability, posterior and vertical retention observed in either dry or wet state. |
| Chan 1991 ²⁴ | Crossover RCT | Not reported | 24 h | 18 complete denture wearers. 4 groups: <ul style="list-style-type: none"> G1 (n=18): Control not treatment. G2 (n=18): Brushing 30 s with <i>Denture Paste</i>. G3 (n=18): Immersion in <i>Efferdent</i> tablet for 12 min. G4 (n=18): Brushing+<i>Efferdent</i> tablet. | <ul style="list-style-type: none"> Colony forming units (CFU) of Anaerobes and <i>Fusobacterium</i>. | Group 3 <i>Efferdent</i> and group 4 Brushing+ <i>Efferdent</i> more effective against Anaerobes and <i>Fusobacterium</i> , although no significant differences between 2 measures. |
| Cruz 2011 ¹³ | RCT | Range: 45-80 | 21 d | 80 complete denture wearers. 4 groups: <ul style="list-style-type: none"> G1 (n=20): Brushing with liquid soap and water+overnight immersion in water. G2 (n=20): Brushing with liquid soap and water+<i>Corega</i> tablet for 20 min+overnight immersion in water. G3 (n=20): G1+Ultrasound for 15 min with <i>Ultrasonic Cleaner</i> after 21 d. G4 (n=20): G2+G3. | <ul style="list-style-type: none"> % internal area of denture covered by biofilm with photographs after staining with dye solution and <i>Image Tool 2.02</i> software | No significant differences in % biofilm between 3 cleaning methods G2, G3, and G4, only between them and control group G1. |
| De Andrade 2011 ¹¹ | RCT | Range: 48-84 | 21 d | 77 complete denture wearers. 4 groups: <ul style="list-style-type: none"> GA (n=25): Brushing+overnight immersion in water. GB (n=29): Brushing+<i>Corega</i> tablet for 20 min+overnight immersion in water. GC (n=28): GA+Ultrasound for 15 min with <i>Ultrasonic Cleaner</i> after 21 d. GD (n=31): GB+GC. | <ul style="list-style-type: none"> Colony-forming units (CFU) of <i>Candida spp</i> and <i>Streptococcus mutans</i> and <i>total aerobes</i>. | Significant reduction of <i>S. mutans</i> in brushing with <i>Corega</i> tablet and by adding ultrasound. Lower total aerobe levels in <i>Corega</i> tablet groups. No significant differences in <i>Candida spp</i> . |
| De Arruda 2021 ²⁵ | RCT crossover | Not reported | 7 d | 45 complete denture wearers. With (n=23) and without immersion (n=22) of the brush also in the solution. 4 groups: <ul style="list-style-type: none"> G1 (n=23): Daily brushing with water and neutral soap+immersion in 0.85% saline solution for 20 min. G2 (n=23): Daily brushing with water and neutral soap+sodium hypochlorite 0.22% for 20 min. G3 (n=23): Daily brushing with water and neutral soap+<i>Efferdent</i> tablet for 3 min. G4 (n=23): Daily brushing with water and neutral soap+<i>Ricinus communis</i> 6.25%. | <ul style="list-style-type: none"> Colony-forming units (CFU) of <i>Candida spp.</i> and <i>S. mutans</i>. % internal area of the denture covered by biofilm with photographs after staining with dye solution and <i>Image Tool 2.02</i> software | No significant differences between 3 cleaning methods G2, G3, and G4, only between them and control group G1. |
| Dills 1988 ²⁶ | RCT crossover | Not reported | Immediate | 14 partial denture wearers. Test I: Ultrasonic cleaning+48 h without brushing. 4 groups: <ul style="list-style-type: none"> G1 (n=14): No treatment. G2 (n=14): Brushing with toothpaste for 30 s (<i>Dentu-Creme</i> toothpaste). G3 (n=14): Immersion in <i>Efferdent</i> tablet for 12 min at 45 °C. G4 (n=14): Brushing with toothpaste (<i>Dentu-Creme</i> toothpaste)+immersion in <i>Efferdent</i> tablet for 12 min at 45 °C. | <ul style="list-style-type: none"> Colony-forming units (CFU) of Anaerobes, in non-selective medium, in selective medium for <i>S. mutans</i>, <i>Fusobacterium</i>, yeast, and <i>Veillonella</i> from denture sample. | No differences between G1 and G2 and between G3 and G4 in CFU in general (nonselective medium), nor in <i>S. mutans</i> , <i>Fusobacterium</i> , yeast, and <i>Veillonella</i> . Significant reductions in G3 and G4 compared with G1 and G2 in general (nonselective medium) and in <i>S. mutans</i> , <i>Fusobacterium</i> , and <i>Veillonella</i> . Not for <i>Ifas</i> . |

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Table 2. (Continued) Characteristics of studies (n=23) of complete denture wearers included in systematic review

| Study (Author/Year) | Type | Age (y) | Duration | Groups | Variables | Conclusions |
|------------------------------|-----------------|--|----------|--|---|---|
| | | | | 16 complete denture wearers. Test II: Ultrasonic cleaning+72 h without brushing. 4 groups: <ul style="list-style-type: none"> G1 (n=16): No treatment. G2 (n=16): Brushing with toothpaste for 30 s (Dentu-Creme toothpaste). G3 (n=16): Immersion in Efferdent tablet for 12 min at 45 °C. G4 (n=16): Brushing with toothpaste (Dentu-Creme toothpaste)+immersion in Efferdent tablet for 12 min at 45 °C. | | |
| Duyck 2013 ²⁷ | RCT Split mouth | \bar{x} : 85.9; DS: \pm 5.9 | 14 d | 51 complete denture wearers. 3 groups: <ul style="list-style-type: none"> G1 (n=18): Overnight immersion in water daily. G2 (n=16): Dry overnight daily. G3 (n=17): Corega tablet overnight daily. | - Total bacterial count and <i>Candida</i> by PCR of denture surface samples. | Significant reductions in bacterial mass and <i>Candida</i> in overnight Corega tablet group compared with overnight immersion in water or dry groups. |
| Duyck 2016 ¹⁵ | Crossover RCT | Not reported | 5 d | 13 complete denture wearers. 4 groups: <ul style="list-style-type: none"> G1 (n=13): Brushing+water overnight daily. G2 (n=13): Brushing+water+Corega tablet overnight daily. G3 (n=13): Ultrasound+overnight immersion in water daily. G4 (n=13): Ultrasound+water+Corega tablet overnight daily. | - Total bacterial count and <i>Candida</i> by PCR of denture surface samples. - % of biofilm | Significantly greater reduction of bacteria overall and of <i>Campylobacter</i> , <i>Streptococcus</i> , <i>Actinomyces</i> , and <i>Veillonella</i> in brushing+Corega tablet group vs brushing alone. Effect more pronounced when ultrasound added (G4). No differences in <i>Candida</i> and % biofilm between groups. |
| Gornitsky 2002 ²⁸ | Crossover RCT | \bar{x} : 84; DS: \pm 8.8 | 21 d | 27 complete maxillary denture wearers. 4 groups: <ul style="list-style-type: none"> Group 1 (n=27): Denture Brite tablet overnight. Group 2 (n=27): Polident tablet overnight. Group 3 (n=27): Efferdent New Concentrated Blue tablet overnight. Group 4 Control (n=27): Overnight immersion in water. | - Colony-forming units (CFU) of <i>Candida</i> spp. and <i>S. mutans</i> . - Visual analogue score for plaque, stains, and food after 7 d. | No significant differences between the 3 cleaning methods in reduction of <i>S. mutans</i> and <i>Candida</i> spp, as well as plaque, staining or food. |
| McAbe 1995 ²⁹ | Crossover RCT | \bar{x} -H 75.7 \bar{x} M 73.8 Range 52-90 | 7 d | 80 complete denture wearers. 4 groups: <ul style="list-style-type: none"> Group G (n=73): Reckitt experimental effervescent tablet with sodium perborate for 10 min without brushing. Group E (n=68): Gentle brushing+Steradent tablet for 10 min in 50 °C water. Group T (n=66): Brushing for 2 min+Colgate Anti-Tartar toothpaste. Group B (n=63): Brushing for 2 min+Cussons Imperial Leather soap. | - Assessment of plaque with dye solution, tartar and stains. | Group E Gentle brushing with Steradent tablet for 10 min in 50 °C water more effective than others in removal of plaque and stains. No differences in calculus removal. |
| Moffa 2011 ³⁰ | RCT | Range 50-75 | 6 mo | 45 complete denture wearers. 3 groups: <ul style="list-style-type: none"> Control group (n=15): Brushing +coconut soap. Perborate group (n=15): Brushing+Corega tablet for 5 min. Chlorhexidine group (n=15): Chlorhexidine Digluconate 2% for 5 min. | - ΔE to measure color changes in Lab coordinates measured at 7, 15 d, 1 mo, 3 mo, and 6 mo. | Color changes observed in Perborate and Chlorhexidine group. Color stability influenced by time. |
| Moffa 2016 ³¹ | RCT | Range 50-75 | 6 mo | 45 complete denture wearers. 3 groups: <ul style="list-style-type: none"> Control group (n=15): Brushing with soft brush+coconut soap 3 times/d. Perborate GP group (n=15): Brushing+Corega tablet for 5 min. | - CFU of microorganisms in culture 48 h and surface roughness measured at 7, 15 d, 1 mo, 3 mo, and 6 mo. | No significant differences between Corega tablet group and chlorhexidine group. From d 15 onwards, no microorganisms observed in dentures in these groups. No differences in roughness between different products. |

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Table 2. (Continued) Characteristics of studies (n=23) of complete denture wearers included in systematic review

| Study (Author/Year) | Type | Age (y) | Duration | Groups | Variables | Conclusions |
|---------------------------------------|---------------|---|-----------|--|--|---|
| | | | | <ul style="list-style-type: none"> Chlorhexidine group (n=15): Brushing+chlorhexidine digluconate 2% for 5 min. | | Roughness decreased over time in all groups. |
| Nalbant 2008 ³² | RCT | \bar{x} : 63.7; Range 43-91 | 7 d | 45 complete denture wearers. 3 groups: <ul style="list-style-type: none"> Group I (n=15): Klorex 0.2% Chlorhexidine. Group II (n=15): Fittydent sodium perborate and sodium bicarbonate tablet. Group III (n=15): Control rinse with water. | - <i>Candida</i> spp. levels, and adhesion of <i>Candida</i> to resin strips. | Klorhex and Fittydent have certain preventive effect on percentage of <i>Candida</i> colonization which changed from 82.2% to 68.8% on denture surface and palatal mucosa, and similar effect on <i>Candida</i> adherence on resin strips |
| Nishi 2014 ¹⁴ | RCT | \bar{x} : 84.6; DS: \pm 8.9; Range 60-101 | Immediate | 50 maxillary and mandibular denture wearers; 100 dentures. 5 groups: <ul style="list-style-type: none"> Group A (n=20): Brushing with water. Group B (n=20): Polident tablet for 15 min. Group C (n=20): Ultrasound with water. Group D (n=20): Brushing+ Polident tablet for 15 min. Group E (n=20): Ultrasound+ Polident tablet for 15 min. | - Colony-forming units of <i>S. mutans</i> , <i>Candida</i> spp., <i>Neisseria</i> spp. in culture medium for 48 h and morphologically identified from a denture sample. | Groups using Polident alone or combined with brushing or ultrasound significantly more effective than brushing or ultrasound alone. Ultrasound+immersion in Polident tablet effectively reduces number of <i>Candida</i> |
| Paranhos 2007 ³³ | Crossover RCT | \bar{x} : 62.3; DS: \pm 9; Range 45-70 | 21 d | 36 denture wearers. 6 groups: <ul style="list-style-type: none"> Group I (n=36): Water. Group II (n=36): Bonyplus tablet alkaline peroxide solution. Group III (n=36): Brushing with Dentu-Creme denture cleaning paste. Group IV (n=36): Combination of II and III. Group V (n=36): Brushing with Oral B soft toothbrush and Dentu-Creme. Group VI (n=36): Combination of II and V. | - % internal area of denture covered by biofilm with photographs after staining with dye solution and Image Tool 2.02 software program | Brushing with Dentu-Creme more effective than using tablet alone. Combination of 2 methods gave more effective results than tablet alone. |
| Peracini 2016 ³⁴ | Crossover RCT | \bar{x} : 60.5; DS: \pm 9; Range 50-80 | 21 d | 32 complete denture wearers. 3 groups: <ul style="list-style-type: none"> Control group (n=32): Water for 8 h. Group AP (n=32): Bonyplus alkaline peroxide solution. Group SH (n=32): Sodium hypochlorite solution 0.5%. | - % internal area of the denture covered by biofilm with photographs after staining with a dye solution and Image Tool 3.0 software. | 0.5% sodium hypochlorite solution most effective method of biofilm removal. |
| Peracini 2017 ³⁵ | Crossover RCT | \bar{x} : 60.5; DS: \pm 9; Range 50-80 | 21 d | 32 complete denture wearers. 3 groups: <ul style="list-style-type: none"> Control group (n=32): Water for 8 h. Group AP (n=32): Corega tablet alkaline peroxide solution. Group SH (n=32): Sodium hypochlorite solution 0.5%. | - CFU of <i>Candida</i> spp. - ΔE to measure color changes. - Surface roughness and bending strength. | Significant reduction of <i>Candida</i> spp. with both solutions. Immersion in AP caused greatest color change, no difference in roughness, but immersion decreased bending strength. |
| Ramage 2019 ³⁶ | Crossover RCT | \bar{x} : 68.7; DS: \pm 5.1; Range 60-75 | 7 d | 19 complete denture wearers. 2 groups: <ul style="list-style-type: none"> Group 1 (n=19): Corega tablet for 15 min+brushing daily Group 2 (n=19): Corega tablet for 15 min+brushing only on the seventh day of the week. | - CFU of microorganisms in dental plaque and microbial composition determined by PCR. | Daily denture cleaning regimes more effective than intermittent ones. |
| Sheen and Harrison 2000 ³⁷ | RCT | \bar{x} :74.4; Range 60-87 | 14 d | 35 complete denture wearers. 2 groups: <ul style="list-style-type: none"> G1 (n=17): Fixodent tablet (with a silicone polymer) dissolved in denturette device for 15 min+Brushing for 30 s G2 (n=18): Immersion in water for 15 min+Brushing for 30 s | - Mean plaque score difference visually and with digital image analysis on day 2 and at the end of the study. | Fixodent tablet group showed significant reductions in plaque (51%) on day 2 and at end of study (42%) compared with control. |
| Silva-Lovato 2010 ³⁸ | RCT | \bar{x} :62.3; DS: \pm 9 | 21 d | 40 complete denture wearers. 2 groups: <ul style="list-style-type: none"> G1 (n=20): Brushing 3 \times d+ immersion in water | - Percentage of biofilm-stained surfaces photographed using imaging software. | Significant reduction in percentage of biofilm and CFU of <i>Candida</i> in the brushing+Medical Interporous |

(continued on next page)

Table 2. (Continued) Characteristics of studies (n=23) of complete denture wearers included in systematic review

| Study (Author/Year) | Type | Age (y) | Duration | Groups | Variables | Conclusions |
|--|---------------|--------------|----------|--|---|--|
| | | | | <ul style="list-style-type: none"> G2 (n=20): Brushing+Medical Interporous denture tablet for 15 min/d. | - CFU of <i>Candida</i> | denture tablet group compared with brushing and water immersion group alone. |
| Srinivasan and Gulabani 2010 ³⁹ | RCT crossover | ̄:65.9 | 14 d | 24 complete denture wearers. 2 groups: <ul style="list-style-type: none"> G1 (n=24): Corega tablet G2 (n=24): Corega tablet+ Chlorhexidine 0.2% rinse. | - CFU after incubation of denture surface samples for 48 hours in culture medium. | Significant reduction in number of bacteria in both groups. Only in first period before washout period differences found between G1 and G2. |
| Tarbet 1984 ⁴⁰ | RCT | Not reported | 3 mo | 75 complete denture wearers. 3 groups: <ul style="list-style-type: none"> Group A (n=24): Efferdent tablet. Group B (n=25): Polident tablet Group C (n=26): Brushing+ Complete cleaning paste. | - Amount of plaque every 7 d for 12 wk. | Method of brushing with cleaning paste consistently most effective in removing plaque from denture. However, whitening effects of effervescent tablets could be useful in hygiene program. |

significant for *Candida* spp. reduction.^{11,13} Nevertheless, other studies^{25,28,32,35,38} confirmed the effectiveness of effervescent tablets (Efferdent, Denture Brite, Polident, Fittydent, Medical Interporous denture, or Efferdent New Concentrated Blue) used daily in conjunction with brushing in reducing *Candida* spp.

When chlorhexidine digluconate was used at different concentrations compared with tablets or brushing with soap or combined with the use of tablets,^{30,31,36,39} no significant reduction of microorganisms was observed. However, the use of 0.2% chlorhexidine (Klorex) was reported to have a preventive effect on the percentage of colonization of *Candida* spp. on the surface of the denture and palatal mucosa, similar to that of the perborate and sodium bicarbonate tablets (Fittydent).³⁶

The use of 0.5% NaOCl appears to be an effective chemical method of biofilm reduction compared with tablets (Bonyplus), with similar results of effectiveness against *Candida* spp. reduction when Corega tables and 0.5% NaOCl were used.³⁴ De Arruda et al²⁵ reported no significant differences in the CFU of *Candida* spp. and *S. mutans* nor in the percentage of biofilm formation using 0.22% NaOCl versus Efferdent tablets with brushing or *Ricinus communis* with brushing.

The use of ultrasonic cleaning has been recommended as an adjuvant mechanism in the cleaning of removable prostheses.¹³⁻¹⁵ However, the combination of brushing and tablets together with ultrasonic cleaning every 21 days has been reported to be no more effective than the daily use of tablets (Corega)¹³ or tablets (Corega, Polident) together with brushing^{14,15} in reducing bacteria and *Candida* spp. However, Nishi et al¹⁴ added another option by incorporating a Polident solution into the ultrasonic bath and reported a significantly reduced *Candida* spp. population with this procedure.

Changes in dimensional stability were not found after overnight storage in dry or in a solution of alkaline peroxide tablets (Kukident).²³ Keeping the dentures

overnight in NaOCl or alkaline peroxide solutions (Corega) could degrade the components of the acrylic resin and lighten its color.³⁵ In 2011, the American Society of Prosthodontics published recommended guidelines for the hygiene of dentures, indicating their storage in water after cleaning.⁷ The systematic review by Verhaeghe et al⁴¹ on denture preservation recommends cleaning the denture at night to reduce *Candida* colonization or at least immersion in an alkaline tablet solution. If the denture is not cleaned at night, the recommendation was to keep it dry to reduce the risk of *Candida* colonization.

The quantitative data from the study were as follows. In the first meta-analysis (Fig. 5A), data from 4 studies^{13,15,37,38} using different scales (visual plaque score and percentage biofilm on the denture surface) were combined with a total of n=70 participants in the brushing+tablet group versus n=71 participants in the brushing group, using a random-effects model by the inverse variance method. Heterogeneity was high (Q-test=41.7; $P<.001$; $I^2=92.8\%$). The meta-analysis estimated a large effect of the combination of brushing with tablet on the reduction of plaque or biofilm on the denture surface ($P=.012$; mean difference=-1.92; 95% confidence interval=-3.45 to -0.38).

To estimate the reduction in the total bacteria level, 3 studies (n=47 in the brushing+tablet group versus n=47 in the brushing group) were combined by using a random-effects model because of high heterogeneity (Q-test=55.6; $P<.001$; $I^2=96.4\%$).^{15,24,26} A "large" effect size was obtained for the combination of brushing with tablet ($P<.001$; mean difference=-4.43; 95% confidence interval: -8.29 to -0.55) (Fig. 5B).

Three studies (n=49 in the brushing+tablet group versus n=49 in the brushing group) were combined to assess the reduction of *Candida* or fungal levels in the denture by using a fixed-effects model, as no heterogeneity was detected (Q-test=0.339; $P=.844$; $I^2=0\%$).^{15,26,27}

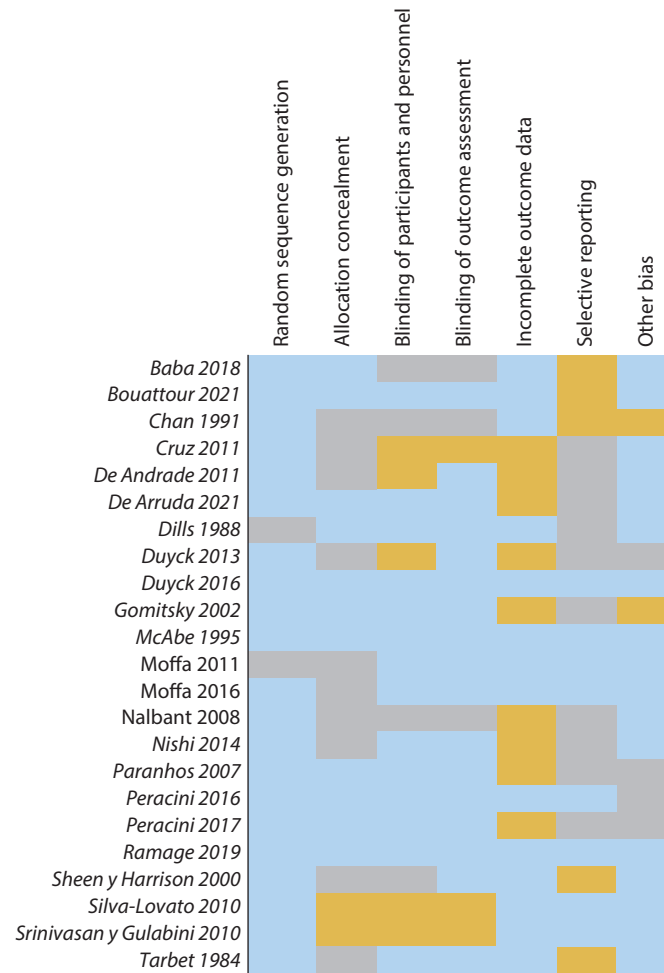


Figure 2. Risk of intrastudy bias (n=32) according to Cochrane tool. *Blue*, low risk. *Gray*, unclear risk. *Orange*, high risk.

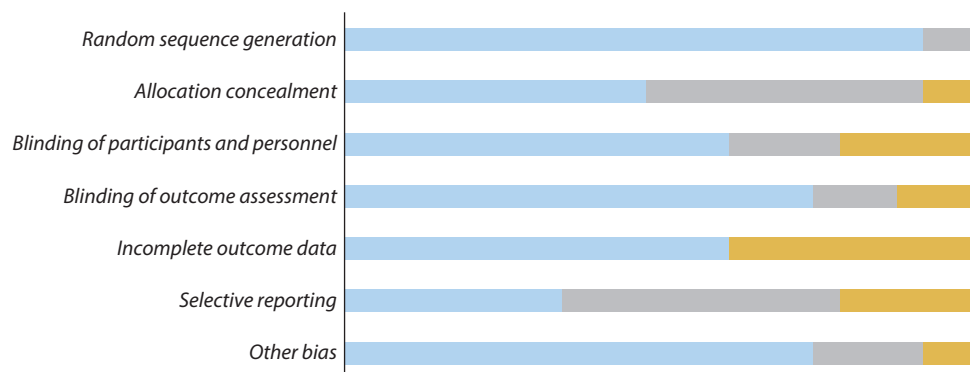


Figure 3. Interstudy risk bias (n=32) per item assessed according to Cochrane tool. *Blue*, low risk. *Gray*, unclear risk. *Orange*, high risk.

A moderate effect size was obtained for the combination of brushing with tablet ($P < .001$; mean difference = -0.78; 95% confidence interval = -1.19 to -0.37) (Fig. 5C).

Publication bias was not detected in any of the 3 meta-analyses using different methods. The Duval and

Tweedie trim-and-fill method did not add any new studies to correct possible asymmetry in the funnel plot, and the estimates did not change. The linear regression method intercept also showed no significance for plaque accumulation ($P = .198$; intercept = -11.2; 95% confidence

Table 3. Methodological quality of 23 included studies using PEDro scale

| Study (Author/Year) | 1. Specified Selection Criteria | 2. Random Allocation | 3. Hidden Allocation | 4. Principle of Comparability | 5. Blinding of Participants | 6. Blinding of Therapists | 7. Blinding of Evaluators | 8. Loss of Participants <15% | 9. Intention-to-Treat Analysis | 10. Statistical Comparisons Between Groups | 11. One-Off Measures and Their Variability | Total Quality Score (Sum of Items 2-11) |
|--|---------------------------------|----------------------|----------------------|-------------------------------|-----------------------------|---------------------------|---------------------------|------------------------------|--------------------------------|--|--|---|
| Baba 2018 ⁸ | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6 |
| Bouattour 2021 ²³ | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 9 |
| Chan 1991 ²⁴ | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 5 |
| Cruz 2011 ¹³ | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 5 |
| De Andrade 2011 ¹¹ | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 6 |
| De Arruda 2021 ²⁵ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 9 |
| Dills 1988 ²⁶ | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 9 |
| Duyck 2013 ²⁷ | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 6 |
| Duyck 2016 ¹⁵ | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 7 |
| Gornitsky 2002 ²⁸ | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 7 |
| McAbe 1995 ²⁹ | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 8 |
| Moffa 2011 ³⁰ | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 7 |
| Moffa 2016 ³¹ | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 8 |
| Nalbant 2008 ³² | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 5 |
| Nishi 2014 ¹⁴ | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 6 |
| Paranhos 2007 ³³ | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 7 |
| Peracini 2016 ³⁴ | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 9 |
| Peracini 2017 ³⁵ | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 8 |
| Ramage 2019 ³⁶ | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 9 |
| Sheen and Harrison 2000 ³⁷ | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 4 |
| Silva-Lovato 2010 ³⁸ | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 4 |
| Srinivasan and Gulabini 2010 ³⁹ | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 6 |
| Tarbet 1984 ⁴⁰ | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 4 |

PEDro, physiotherapy evidence database.

interval=-36.7 to 14), for bacterial count ($P=.117$; intercept=-11.5; 95% confidence interval=-38.0 to 15.7), or for *Candida* reduction ($P=.979$; intercept=0.12; 95% confidence interval=-48.9 to 49.2). The fail-safe numbers were 60, 73, and 8, respectively. The funnel plots are shown in Figure 5D-F.

Based on the results of the 3 meta-analyses, the use of tablets together with brushing achieved a large effect in the reduction of biofilm and bacteria levels and a moderate effect in *Candida* levels compared with

brushing alone. Recommendations with a strong level of evidence can be established and are presented in Table 4.

DISCUSSION

The null hypothesis was rejected. The rank of evidence of this systematic review and meta-analysis was assessed by the grading of recommendations, assessment, development, and evaluation system scale. The risk-benefit ratio,

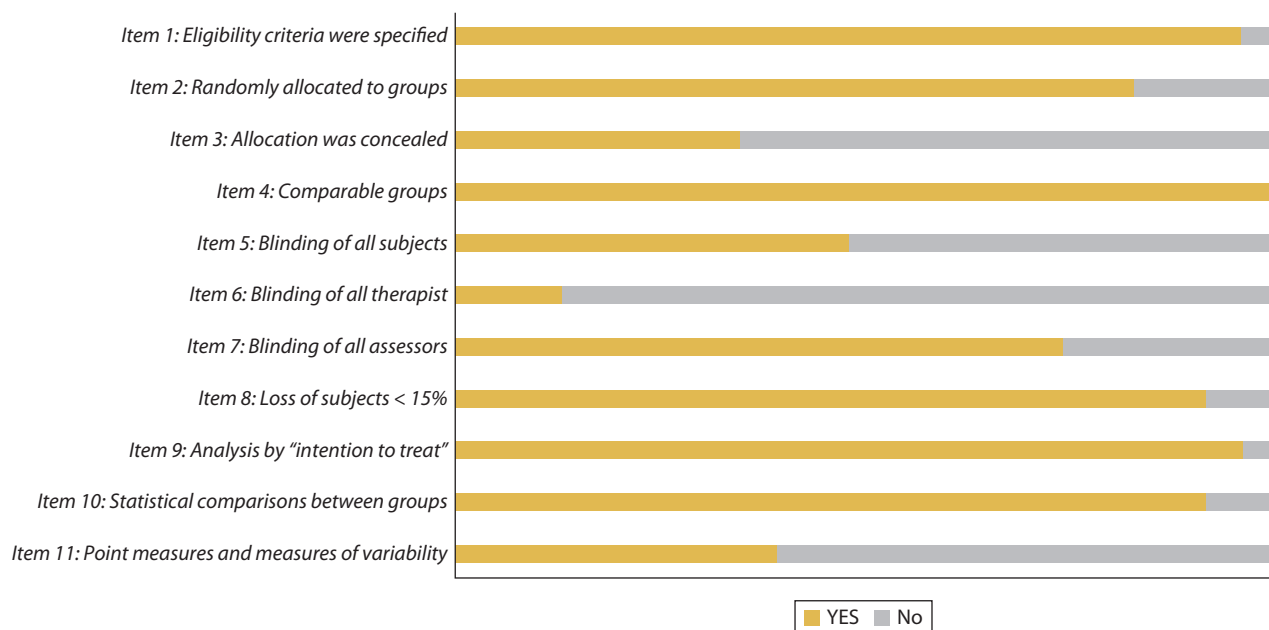


Figure 4. Interstudy quality (n=32) per item scored according to PEDro scale. PEDro, physiotherapy evidence database.

application under specific conditions, and the quality of the evidence were considered.

In addition to the assessment of bias and quality of the studies, the heterogeneity in aspects such as participant characteristics, background, and age of participants should be noted. Other heterogeneous factors were the procedures tested, products, application times, and combinations of procedures, as well as the monitoring times in each group.

With regard to application times, 2 authors^{14,26} quantified microorganisms in CFU/ml with a single application of the different protocols evaluated. However, Moffa et al^{30,31} conducted a 6-month follow-up. These authors did not find significant differences in the groups that used Corega or chlorhexidine immersion of the denture daily for 5 minutes after 15 days of follow-up or longer, so the minimum follow-up time for assessing the microbial load of the denture should be set at 15 days. Regarding the time of immersion in the disinfectant solutions,^{8,11,15,23,27,28,30,32,34,35,39} times ranged between 2 and 20 minutes to overnight.

The 3 meta-analyses conducted^{6,13,15-17,24,26,37,38} have focused on assessing the effect of adding an effervescent cleaning tablet to the usual practice of daily denture brushing, confirming a large effect on the reduction of biofilm and microbial load, as well as a moderate effect on *Candida* levels. To analyze the efficacy of the tablet on biofilm accumulation, 4 studies were combined,^{13,15,37,38} with follow-up periods between 14^{15,37} and 21 days.^{13,32} The tablets used were Fixodent,³⁷ Medical Interporous Denture,³⁸ and Corega.^{13,15} The meta-analysis confirmed the significant plaque and biofilm reducing effect of the tablets when added to denture brushing.

In the study of the effect on the microbial load, 3 studies were combined, 2 of them measuring CFU^{24,26} and the other measuring the total bacterial count by polymerase chain reaction.¹⁵ The follow-up time was immediate,²⁶ 24 hours,¹⁵ or 5 days,²⁴ respectively. The studies were conducted with Efferdent^{24,26} and Corega,¹⁵ and a significant reduction of microorganisms was detected when combining brushing and tablets.^{6,16,17}

Finally, to assess the effect on *Candida*, 3 studies were combined.^{15,26,32} Monitoring times ranged from immediate,²⁶ to 5 days,¹⁵ to 21 days,³⁸ respectively. The tablets evaluated were Efferdent,²⁶ Medical Interporous Denture,³⁸ and Corega.¹⁵ The meta-analysis did not show heterogeneity. From the 3 studies combined, 2 had a significant effect.^{26,38} This allows confidence in estimating a moderate effect size in reducing *Candida* levels.

Strengths of this systematic review included the use of a significant number of keywords and descriptors in the search strategy in 5 different databases, covering most of the scientific literature published on the subject. In addition, the eligibility criteria focused on the study design with the highest level of evidence, which were randomized and nonrandomized controlled clinical trials. Although most of the studies had small sample sizes, which made it necessary to carry out studies with a crossover design, the selection of patients complied with the principle of representativeness, which provided adequate external validity. Limitations included the large number of studies with incomplete outcome data together with high heterogeneity, which did not facilitate larger meta-analyses

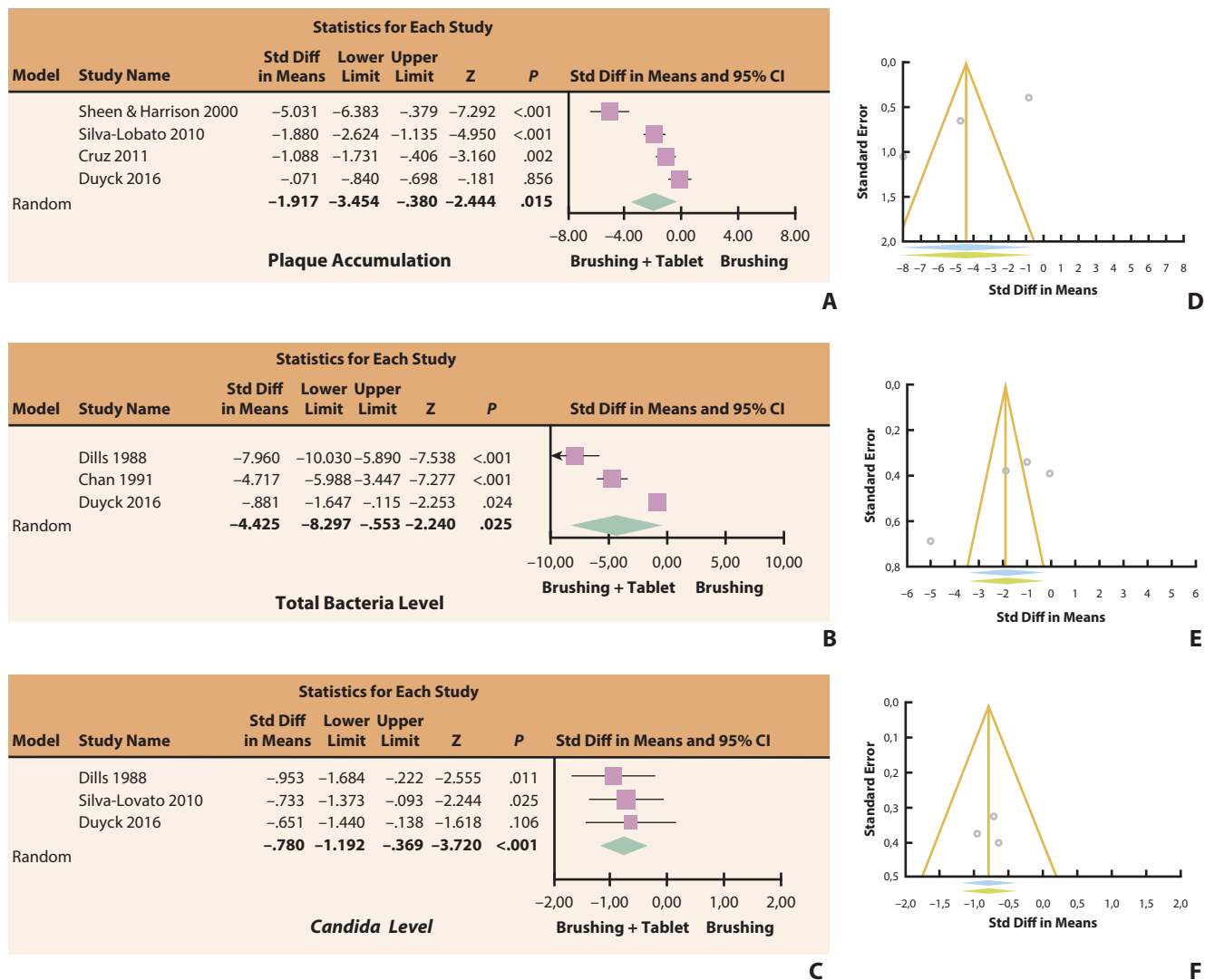


Figure 5. A, Forest plot of meta-analysis of plaque reduction between combined method of brushing+tablet versus brushing. B, Forest plot of meta-analysis total bacteria level reduction between combined method of brushing+tablet versus brushing. C, Forest plot of meta-analysis of *Candida* levels reduction between combined method of brushing+tablet versus brushing. D, Funnel plot of meta-analysis of plaque reduction between combined method of brushing+tablet versus brushing. E, Funnel plot of meta-analysis total bacteria level reduction between combined method of brushing+tablet versus brushing. F, Funnel plot of meta-analysis of *Candida* levels reduction between combined method of brushing+tablet versus brushing.

that would have provided more scientific evidence; for this reason, many 2-by-2 comparisons and net-meta-analyses could not be performed.

CONCLUSIONS

Based on the findings of this systematic review and meta-analysis, the following conclusions were drawn:

1. Strong evidence was found that the use of effer- vescent tablets in conjunction with brushing had a significant effect on biofilm reduction and on microbial levels when compared with brushing alone.
2. Insufficient evidence was found that one chemical method is better than another, as there was

Table 4. Recommendations for cleaning removable prosthesis appliances

- Brushing of the prosthesis, followed by daily immersion according to manufacturer’s instructions in warm water (37 ±2 °C) with cleaning tablet. Overnight immersion in water. (*Recommendation 1A*)
- Brushing of the prosthesis, followed by immersion in 0.5 % sodium hypochlorite for 10 min. Overnight immersion in water. (*Recommendation 1A*)
- In institutionalized patients or patients with limitations for caring for prosthesis, daily brushing, overnight soaking in water and immersion in ultrasonic bath every 21 d with cleaning tablet for 15 min may be recommended as alternative to above. (*Recommendation 1A*)

disparity and lack of homogeneity in the method- ology used. However, all the chemical methods assessed were more effective when combined with brushing.

3. Immersion in an ultrasonic bath every 21 days with water along with daily brushing of the denture was effective in reducing the amount of biofilm and bacteria levels on the denture. The use of tablets in combination with ultrasound was more effective against *Candida*.

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