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A Network Meta-analysis of Interproximal Oral Hygiene Methods in the Reduction of Clinical Indices of Inflammation

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Abstract

Background—A wide selection of Interdental Oral Hygiene (IOH) aids is available to consumers. Recommendations for selection are, however, limited by the lack of direct comparisons in available studies. We aimed to assess the comparative efficacy of IOH aids using Bayesian Network Meta-Analysis (BNMA).

Methods—Two independent reviewers performed a systematic literature review of randomized clinical trials assessing IOH aids, based on a focused question. Gingival inflammation (Gingival Index (GI), Bleeding-on-probing (BOP)) was the primary outcome and plaque and probing depth were secondary outcomes A random-effects arm-based BNMA model was run for each outcome; posterior medians and 95% credible-intervals (CIs) summarized marginal distributions of parameters.

Results—A two-phase selection process identified 22 trials assessing 10 IOH aids as brushing adjuncts. Interdental brushes (IB) yielded the largest reduction in GI (0.23 [95% CI: 0.09, 0.37]) as toothbrushing adjuncts, followed by water-jet (WJ) (0.19 [95% CI: 0.14, 0.24]). Rankings based on posterior probabilities revealed that IB and WJ had the highest probability of being "best" (64.7% and 27.4%, respectively) for GI reduction, while the probability for toothpick and floss being the "best" IOH aids was near zero. Notably, except for toothpicks, all IOH aids were better at reducing GI as compared to control.

Conclusions—BNMA enabled us to quantitatively evaluate IOH aids and provide a global ranking of their efficacy. Interdental brushes and water-jets ranked high for reducing gingival bleeding, while toothpicks and floss ranked last. The patient-perceived benefit of IOH aids is not clear because gingival inflammation measures are physical indicators of periodontal health.

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Keywords

meta-analysis; systematic reviews and evidence-based medicine; oral hygiene; dental hygiene; gingivitis

Introduction

Oral care over-the-counter products recorded nearly $5 billion in sales in 2012, according to a recent market survey.[1] Dental floss, interdental brushes, waterjet devices, toothpicks and other interdental cleaning devices account for a substantial share of the market. Despite this sizeable retail market, relatively little data exists to enable oral health care professionals and consumers to compare among the many available products.[2] In fact, the recent workshop consensus by the European Federation of Periodontology concluded "flossing cannot be recommended other than for sites of gingival and periodontal health, where inter-dental brushes will not pass through the interproximal area without trauma".[3] Given that flossing was previously considered the gold standard for interproximal hygiene,[4,5] these guidelines have further perplexed the selection oral hygiene methods for interproximal cleaning.

The association between interproximal oral hygiene (IOH) habits and reduction in plaque control has been well established[6,7]. However, evidence regarding the most efficacious means of interdental tooth cleaning remains equivocal[8-11]. Clinical studies on the efficacy of IOH aids are often industry-driven and such studies commonly employ a single intervention as compared to tooth brushing alone to test products of interest[12]. Conventional pairwise meta-analysis is a valuable tool for comparing treatment effects between two interventions, but it has its limitations particularly when multiple interventions exist; such as in the case of oral hygiene aids. The authors of a recent meta-analysis sought to compare interdental brushes, flossing, toothpicks, or brushing alone on measures of periodontal inflammation, but were able only to quantitatively evaluate interdental brushes and flossing utilizing conventional meta-analysis modelsl[8]. Conventional pair-wise meta-analyses on this topic remain inconclusive due to the large number of interventions available and the small number of studies that report comparisons with the same intervention groups. Network meta-analysis (NMA) has been introduced in oral health research as an approach that can combine direct and indirect (i.e., those not directly made in individual trials) comparisons among the included studies.[13] For IOH, the application of NMA for assessing the comparative efficacy of various treatments can increase the breadth of studies included in the meta-analysis, as indirect comparisons are possible. In addition, NMA can provide information on the overall ranking of the various interventions, which are easily interpretable and can enhance the communication of results directly to clinicians and the general population. Thus, the aim of this study was to assess the comparative efficacy of IOH aids using Bayesian Network Meta-Analysis (BNMA).

Methods

The following focused question was constructed according to the Population, Intervention, Comparison, Outcome measures (PICO)[16] approach: "For individuals physically able to perform oral hygiene tasks, will any specific means of interproximal tooth cleaning lead to greater reduction in plaque accumulation, gingival inflammation and pocket depth reduction in comparison to other means of interproximal tooth cleaning, or tooth brushing alone?". Reduction in gingival inflammation was assessed as the primary outcome, while reductions in plaque and probing depth were assessed as secondary outcomes. Gingival inflammation was measured by Gingival Index (GI)[14] and Bleeding-on-probing (BOP).[15] Reporting of this study was performed according to PRISMA guidelines (Moher et al. 2009).[16]

Selection Criteria

The criteria for inclusion of studies for this systematic review and network meta-analysis were: i) randomized clinical trials; ii) assessment of IOH methods performed by physically competent persons; iii) report of outcomes measuring gingival inflammation, plaque, or probing depth; and iv) at least 2 weeks of follow-up. Exclusion criteria were: i) uncontrolled clinical studies, non-randomized clinical studies; and ii) less than 10 patients in each study group.

Search Strategy

To identify potentially eligible studies, an initial search of titles and abstracts relevant to the PICO question was performed from 1/1/1980 through 04/17/2015 using three electronic databases: Ovid Medline (including Ovid Medline In-Process), EMBASE, and Web of Science. A combination of keywords, MeSH terms and Boolean operators was utilized for the search. The full search strategy for the Ovid search is provided in Suppl. Table 1. The electronic search was complemented with manual searching of select journals: *Journal of Periodontology, Journal of Clinical Periodontology, The International Journal of Periodontics and Restorative Dentistry and International Journal of Dental Hygiene*. The search was performed independently and in duplicate by two reviewers (G.K. and A.I.) according to AMSTAR[17] guidelines for methodological quality of systematic reviews. Full-text articles were then read independently and in duplicate by the two reviewers for final inclusion based on the predefined selection criteria. In case of disagreement between the two reviewers, the opinion of a third reviewer (M.J.) was considered definitive. Inter-reviewer agreement was recorded at each phase of study selection and assessed with the Cohen's kappa (κ) coefficient.[18]

Data Extraction

Two reviewers (G.K. and A.I.) independently extracted the following data: year of publication, location of data, source(s) of funding, number of participants in each arm, number of interventions, and outcomes for each study. Data were entered in an electronic sheet.

Quality Assessment

Included studies where assessed for bias according to the recommendations of the Cochrane Handbook of Systematic Reviews for evaluation of randomized-controlled trials by two reviewers (G.K. and M.J.). Particularly, we assessed selection bias, performance bias, detection bias, attrition bias and reporting bias. Each study was assigned "Low risk", "High risk", or "Unclear risk" of bias according to previously reported methodology.[19]

Statistical Analysis

Bayesian network meta-analysis—Due to the small sample size reported in most published studies, results from traditional pairwise meta-analyses may not be reliable. In addition, most of the comparisons in previous systematic reviews were based on fewer than 3 studies, which precludes the use of pairwise random effects meta-analyses. Bayesian network meta-analyses (BNMA), also known as mixed treatments comparisons, extends traditional Bayesian meta-analyses of two treatments to simultaneously incorporate the findings from several studies on multiple treatments.[13, 20-23] BNMA borrows strength from indirect evidence, which can improve statistical efficiency and reduce potential bias.

For the present analysis, a random effects arm-based (AB) NMA model[23,24] was utilized for each outcome, allowing the inclusion of all the possible treatment comparisons. The detailed description of the model can be found in the Appendix. Non-informative priors were used for the fixed effects throughout the analysis to minimize the impact of prior information on final results. Weakly informative priors were used for the covariance matrices. JAGS software (version 3.4.0) via the “rjags” package in R software[*] was used to sample from the joint posterior distribution using Markov Chain Monte Carlo (MCMC) methods. The posterior samples were drawn by Gibbs sampling algorithms.[25] The marginal distributions of the parameters of interest were summarized by the posterior medians and 95% credible intervals (95% CIs). Four chains of 100,000 MCMC samples were saved after 50,000 burn-in, and convergence was assessed using trace plots and Gelman-Rudin statistic.[26]

Ranking Interventions—The Bayesian network meta-analysis allowed us to not only assess pairwise but also assess global efficacy ranking among the interventions. The posterior distribution of the rank of each treatment for each outcome was obtained. The probability of each treatment being the best intervention was also calculated. The “best intervention” was identified as the one with the highest estimated posterior probability of ranking first among all the tested interventions.

The ranking probability was sensitive to small changes in the posterior distribution. As another ranking measure that not only uses the first but summarizes all rankings for a particular intervention, the surface under the cumulative ranking was estimated.[9, 27] The larger the SUCRA value for the k_{th} intervention, the higher its overall rank among the available intervention options. SUCRA would equal “1” when an intervention was unequivocally the best, and “0” when an intervention was the worst.

Results

The search strategies identified 615 unique titles and abstracts. Following the first phase of search, 544 articles were excluded as irrelevant to the PICO question (κ score for inter-reviewer agreement [95% Confidence Interval (CI)]: 0.85 [0.78, 0.91]). Assessment of the full-text articles from the remaining 71 articles led to the exclusion of 49 studies after application of the pre-specified exclusion criteria (κ [95% CI]: 0.80 [0.66, 0.95]). In total,

[*] Comprehensive R Archive Network - https://cran.r-project.org/

N=22 clinical trials fulfilled the inclusion criteria and were included in the NMA (Suppl. Figure 1).

Risk of bias assessment of included studies

We evaluated selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias in 22 selected articles.[10,28-48] Four studies were assessed as having a low risk of bias (Rosema, 2011; Zimmer, 2006; Mythri, 2015; Jackson, 2006;),[10, 28-30] while one study as having high risk of bias (Walsh, 1989).[31] The remaining included studies were judged as having unclear risk of bias. Results are presented in Suppl. Figure 2.

Study characteristics

The present systematic review identified 22 randomized trials that investigated 18 interventions or combinations thereof against toothbrushing controls.[10, 28-48] The interventions could be further grouped into 10 major IOH method categories including flossing (FL), powered flossing (FL2), toothpicks (TP), toothpicks and intensive oral hygiene instructions (TO), water jet irrigation devices (WJ), interdental brushes (IB), gum massaging devices (MD), toothbrush only (Ctrl), powered, electric, sonic toothbrush (Powered Ctrl), Powered control and water jet (PW) (Table 1). Number of participants per study arm ranged from N=10 (Kazmierczak et al. 1994)[37] to N=110 (Bauroth et al. 2003).[33] All of the included studies reported on reduction in gingival inflammation; the majority utilized the modified Quigley index while two studies (Walsh et al. 1985, Rosema et al. 2011)[10,35], only reported percentages (%) of sites that bled on probing (BOP). Regarding plaque removal, two studies only provided plaque control record data (% PCR)[49] (Walsh et al. 1985, Goyal et al. 2012)[35,36] and the remaining studies reported the categorical plaque index (PI)[14]. Due to the small number of studies utilizing PCR, these were excluded from data synthesis for this secondary outcome. Only three studies (Kazmierczak et al. 1994, Barnes et al. 2005, Jackson et al 2006)[30,37,42] reported probing depth changes post-intervention. Nine of the included studies (40.9%) were industry-funded[29-34,36,41,48] with the remaining studies not reporting funding (Table 2).

Results of NMA

As mentioned above, the interventions reported in the N=22 included studies were grouped into 10 group nodes. Figure 1 demonstrates the network plots for the primary outcome using two measures (GI, BOP). The network plots revealed that the maximum number of inter-group direct comparisons was N=6 for the comparison between FL and Ctrl, while the majority of direct comparisons were limited to one or two studies. These plots exemplify the significance of enabling indirect comparisons by utilizing a network meta-analysis framework (Figure 1). Overall, the grouping of studies in 10 nodes allowed for 36 pairs of comparisons for PI and GI and 45 pairs of comparisons for BOP (Figure 1, Suppl. Fig. 3). Due to the small number of studies reporting on PD changes, the NMA only included 3 pairwise (2 direct and 1 indirect) comparisons for this outcome (Suppl. Fig. 4).

Toothpick with intensive oral hygiene instruction (TO) achieved the greatest BOP reduction in comparison to control (26.4% [95% CI: 7.50, 45.4]). The second greatest additional reduction in BOP against control was noted for waterjet (WJ) with an average of 19.3%

(95% CI: 16.2%, 22.4%) (Table 3). Floss (FL) and automated floss (FL2) were also significantly more effective than control in reducing BOP, but the effect size was relatively small for both interventions (FL 95% CI: 5.1%, 10.3%, FL2 95% CI: 2.0%, 11.2%). Notably, IB yielded the highest reduction in GI with a mean of 0.23 (95% CI: 0.09, 0.37). WJ had the second largest effect with a mean reduction of 0.19 (95% CI: 0.14, 0.24). For reduction in PI, IB was more efficacious than the majority of the alternative oral hygiene aids with a mean effect of 0.34 reduction in GI as compared to control (95% CI: 0.12, 0.56) (Table 3). Notably, only six of the 21 comparisons between active treatments (not involving Ctrl or Powered Ctrl) were statistically significant different than zero for BOP reductions.

Treatment ranking

Ranking results were similar when computed probabilities or SUCRA values were used (Table 4). For BOP reduction, TO and WJ were most likely to be categorized the best amongst all interventions (70.4% and 12.6%, respectively). IB showed the largest probability for being the best intervention for reducing GI with 64.7% chance followed by WJ (Table 4, Figure 2). The highest SUCRA value for PI was 95.5% for the IB followed by PW. IB also ranked 1st for PD reduction with the second intervention having almost half its SUVRA value. Results of intervention ranking showed that IB and WJ consistently ranked high among all intervention, while TO was more likely to rank 1st for BOP reduction (Suppl. Figure 5-8).

Discussion

The present BNMA enabled us to quantitatively evaluate OH aids and provide a global ranking of their efficacy. Among 10 IOH aids, interdental brushes and water-jets ranked high among the aids for reducing gingival bleeding. Unsupervised flossing did not yield substantial reductions in gingival inflammation. The present findings are aligned with the recommendations set forth following a consensus meeting during the 11th European Workshop in Periodontology[3] that forced the periodontal community to rethink the recommendation for flossing across groups and levels of periodontal health. The present work corroborates the recommendations derived from the workshop proceedings, which state that flossing cannot be generally recommended for managing gingivitis except for sites where the interdental space is too limited to allow the passage of an interdental brush without trauma. In fact, our meta-analysis did not limit the selection to interproximal hygiene aids to interdental brushes and floss but also suggested that water-jet devices and potentially toothpicks, when used under intensive oral hygiene instruction, may be beneficial homecare aids in the management of gingivitis. Given the prevalence of gingivitis, providing the general public with efficacious alternatives to flossing would likely have significant public health impact.

Flossing has received the most attention among IOH aids and is highly recommended by dentists and dental associations alike due to its conceptually superior capability of removing plaque for interdental areas.[50] Therefore, a word of caution regarding the interpretation of findings from the present study is important. The present NMA does not refute the efficacy of flossing for removing interproximal plaque around teeth. The challenge of performing a technically-demanding OH habit[51] such as flossing may help explain it's relatively poor ranking against other IOH aids. When performed effectively, flossing is likely an efficacious approach against gingival inflammation and potentially dental caries.[52] For example, one study confirmed that daily (weekdays) professional flossing can prevent the incidence of caries in schoolchildren by 40%.[52] Nevertheless, trials assessing the efficacy of self-administered flossing and dental caries have largely failed to show any effect.[53] These findings support the hypothesis that flossing is indeed efficacious, but its effective application is elusive. Our results support that dental floss is not the quintessential IOH method. Persons that are effectively using floss should not be instructed to discontinue their OH habits. Importantly, as suggested by our findings, other OH adjuncts actually have an increased likelihood of being effective in reducing gingival inflammation, such as interdental brushes, waterjet devices and dental toothpicks with the appropriate OH instruction.

A strength of the present study that allowed the comparison of multiple interventions despite the limited number of studies offering direct comparisons lies in the use of a random effects arm-based NMA model.[5, 6, 23, 24] This model allowed the inclusion of all the possible treatment comparisons in the meta-analyses for each of the outcomes as compared to previous meta-analyses that were limited by the inclusion of only direct estimates in their models.[54,55] Nonetheless, a limitation of our study is that existing NMA models are restricted to the asynchronous assessment of each of the outcomes. This limitation confounds the interpretation of the results to the extent that treatment ranking varies across models.

The ranking of interventions also differed according to the outcome selected. For example, interdental brushes and toothpicks ranked highest for reductions in plaque (PCR) and gingivitis (BOP), respectively. The lack of modelling techniques allowing the simultaneous assessment of multiple outcomes in meta-analyses hampers our ability to draw more definitive conclusions when multiple outcomes are considered similarly relevant. Finally, in future studies it would also be relevant to include safety outcomes, such as gingival trauma and patient-related outcomes in the global ranking, which could not be captured in the present study.

Further limitations of the present study were the small number of studies involving certain interventions, and the heterogeneity in the sample populations and the methods of IOH instruction. Walsh et al. (1985)[35] utilized toothpicks followed by intensive oral hygiene instruction in one arm of a multi-arm clinical trial. This group performed very well in terms of reduction in bleeding on probing as compared to other test groups and as a result following indirect comparisons for model estimation this intervention was ranked as having the highest probability of being the best for BOP reduction. However, inclusion of only one study with this intervention warrants cautious interpretation of the results as it is unclear whether the benefit was due to the use of the IOH aid or the intensive oral hygiene instruction employed in this study. Furthermore, the lack of information related to participants' periodontal status in a large number of included studies precluded drawing any conclusions related to the performance of various aids in persons with a pristine versus a reduced periodontium. It has been well known that the proximal attachment loss observed in periodontitis alters the topography of the interdental region and modifies the performance of

IOH aids.[56] Christou et al.[56] reported that in persons with periodontitis, use of floss led to 50% less reduction in plaque levels as compared to use of interdental brushes. One plausible explanation is the lack of papillary guidance. The design of the dental floss has been grounded upon the presence of a soft tissue peak in the pyramidal proximal space that separates the sulcular epithelia of two adjacent teeth. On the other hand, the interdental brush requires a certain space availability to enter the interdental region and remove plaque. Lastly, gingival inflammation is a physical indicator of oral health, but patient-oriented outcomes are preferred for clinical decision-making.[57] Comprehensive patient-oriented concepts such as oral health-related quality of life would allow to measure the total effect on the patients' perceived oral health, not only on specific parameters of gingival health.

Conclusion

In summary, our network meta-analysis demonstrated that unsupervised flossing does not yield substantial reduction in gingival inflammation. Among 10 IOH aids, interdental brushes and water-jets ranked high among other aids for reducing gingival bleeding. Selection of a single IOH aid as the gold standard is not possible based on existing data as their effectiveness depends on ease of use, appropriate instruction and interdental anatomy and periodontal status. Most importantly, the patient-perceived benefit of the IOH aids is not clear because most studies investigated disease-oriented outcomes of gingival health, providing only limited information what matters to patients.

In the absence of strong evidence about IOH aids differences in the impact on patients, practitioners should customize IOH aid recommendations and offer alternatives rather than insisting on instruction on the use of a universally recommended cleaning aid. Further well designed and appropriately powered clinical trials are warranted to provide more authoritative guidelines on IOH selection.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

Model description

Let $\bar{y}_{ikl}$, σ^2_{ikl} and n_{ikl} denote the observed aggregated outcome, the estimated sample standard deviation, and the sample size from study i for treatment k and outcome l, respectively, where $i = 1, \ldots, 22$, $k = 1, \ldots, 10$, $l = 1$ indicates baseline measure and $l = 2$ indicates endpoint measure. We assume that the observed outcome $\bar{y}_{ikl}$ follows a normal distribution with group-specific true mean θ_{ikl} and variance σ^2_{ikl}/n_{ikl}, i.e., $\bar{y}_{ikl} \sim N\left(\theta_{ikl}, \sigma^2_{ikl}/n_{ikl}\right)$. We adopt a random effect models for θ_{ikl}, which can be described as following:

$$\theta_{ikl} = \mu_{kl} + v_{ik} + w_{il},$$

where μ_{kl} is the fixed mean effect of treatment *k* for outcome *l*. The parameters $v_{ik}$and w_{il} are two independent study-specific random effects that account for the heterogeneity in treatment effects and outcomes across the trials, respectively. We assume that $v_{ik} = \left(v_{i1}, v_{i2}, \cdots, v_{iK}\right)^T \sim N_K(0, \Sigma)$ and $w_{il} = \left(w_{i1}, w_{i2}\right)^T \sim N_2(0, \Lambda)$. The covariance matrix Σ captures the possible correlations between the K treatments, whilst the covariance matrix Λ captures the correlation between the baseline and endpoint measurements. Here, we treat the aggregated baseline and endpoint value as two separate outcomes for each study, since we do not have information on the estimated variance of the difference between these two measurements in each study. The relative treatment effect between treatment *b* and treatment *k* can be summarized as $d_{bk} = (\mu_{b2} - \mu_{b1}) - (\mu_{k2} - \mu_{k1})$. We place non-informative normal priors N(0,1000) on the fixed effects. We assign inverse Wishart priors on the covariance matrices: $\Sigma \sim IW\left(R_1, df_1\right)$ and $\Lambda \sim IW\left(R_2, df_2\right)$. The parameters in the inverse Wishart priors are selected to ensure relatively diffuse prior distributions on the covariance matrices, but not assign excessive probability on very large (unrealistic) values. Specifically, the degrees of freedom df_1 and df_2 are chose to be the dimensions of Σ and Λ, respectively. The off-diagonal elements of R1 and R2 are 0.005, while diagonal elements are equal to 1.

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One-sentence summary

Interdental brushes and water-jets rank high for reducing gingival bleeding, while floss ranks last.

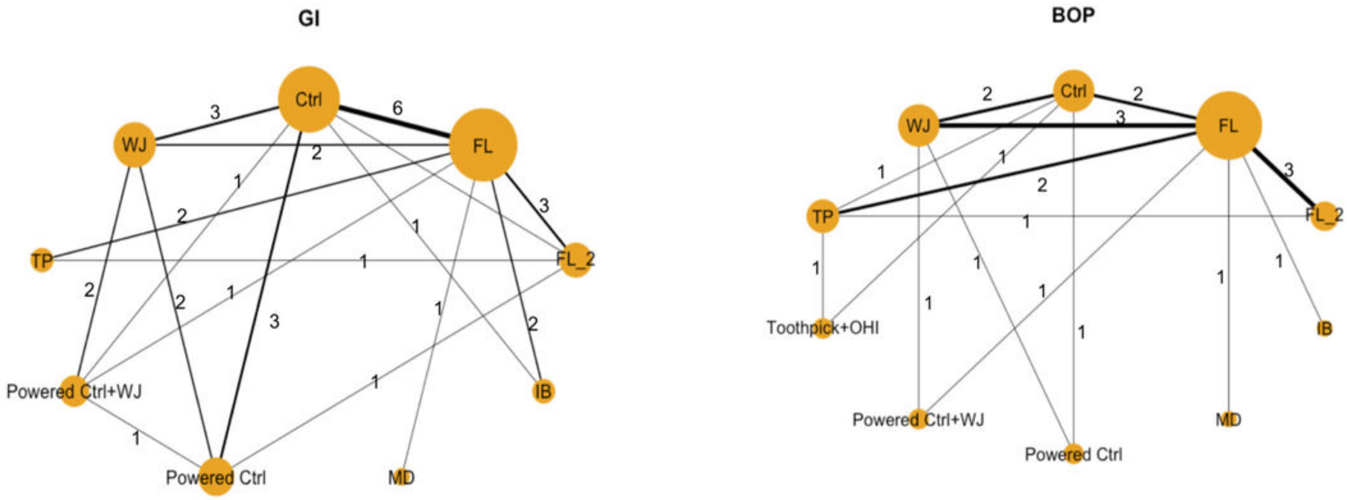
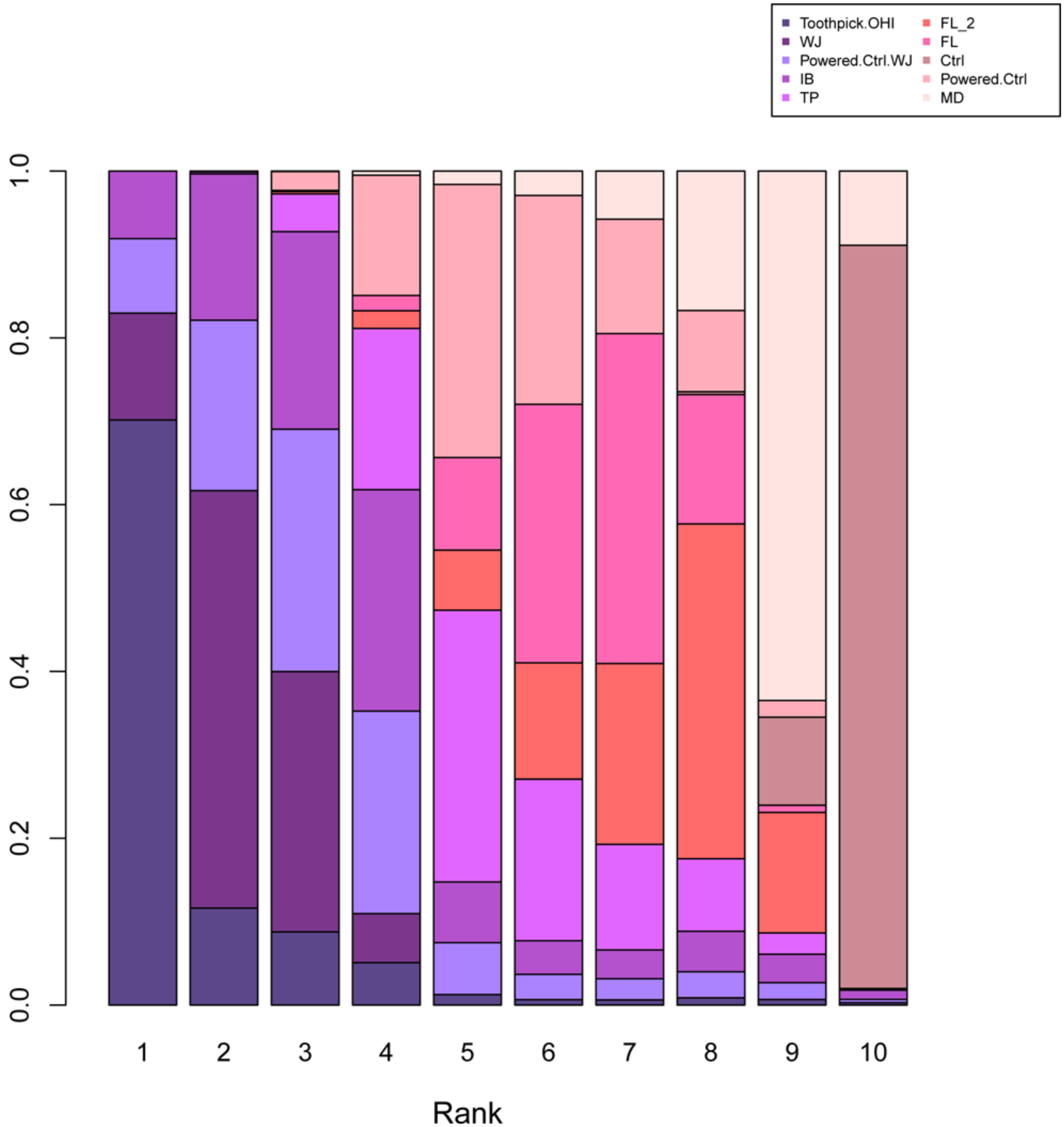


Figure 1.

Network plots of the studies assessing gingival inflammation (primary outcome) with either of two measures: either as Bleeding on probing (BOP) or Gingival Index (GI). The nodes represent the interventions, and edges connecting two nodes indicate that the direct evidences of the corresponding intervention comparisons. The node size is proportional to the number of studies that include the corresponding intervention. The thickness of the edge is proportional to the number of studies that directly compare the corresponding pair of interventions.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WJ
Powered.Ctrl.WJ
IB
TP
FL_2
FL
Ctrl
Powered.Ctrl
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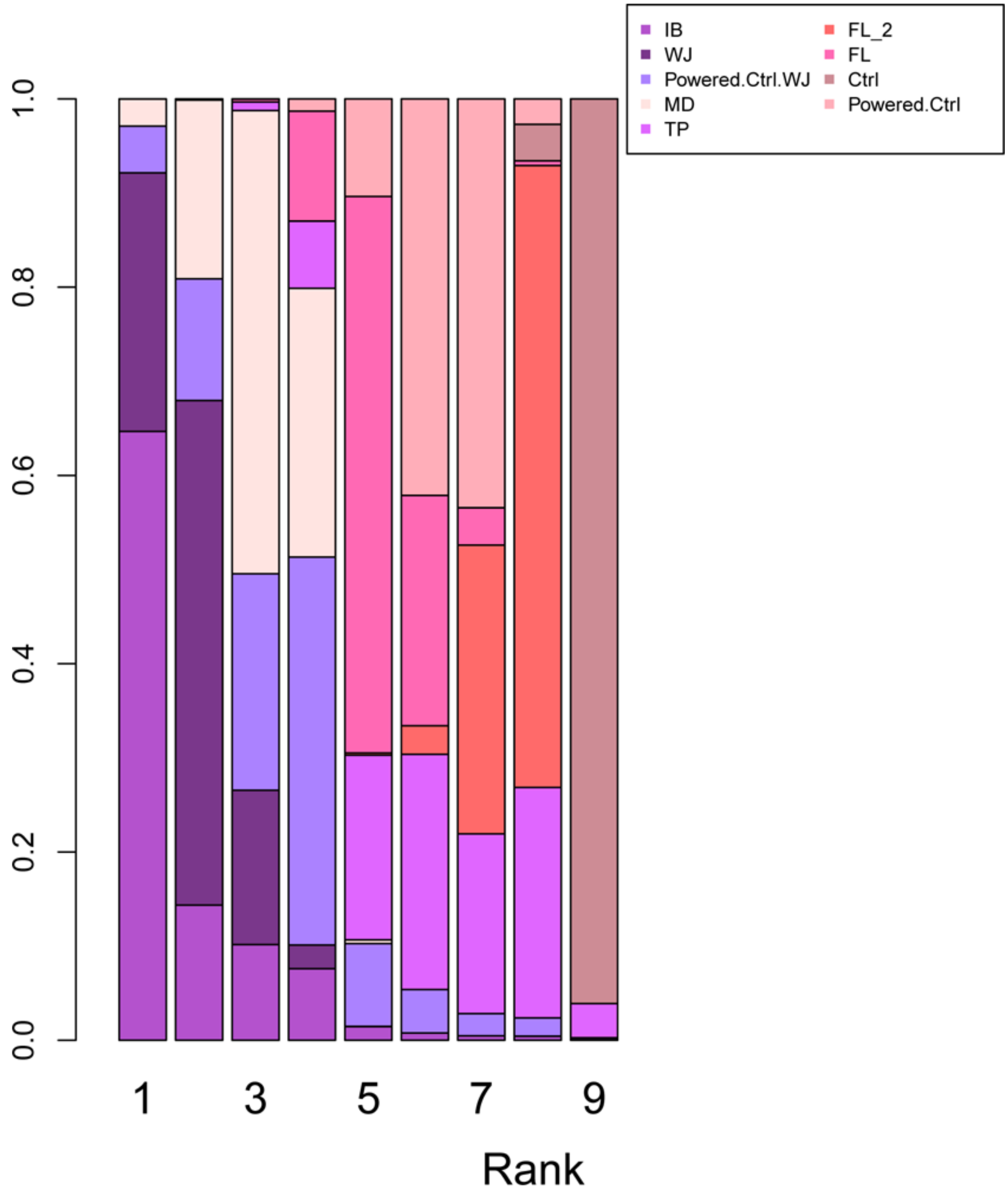
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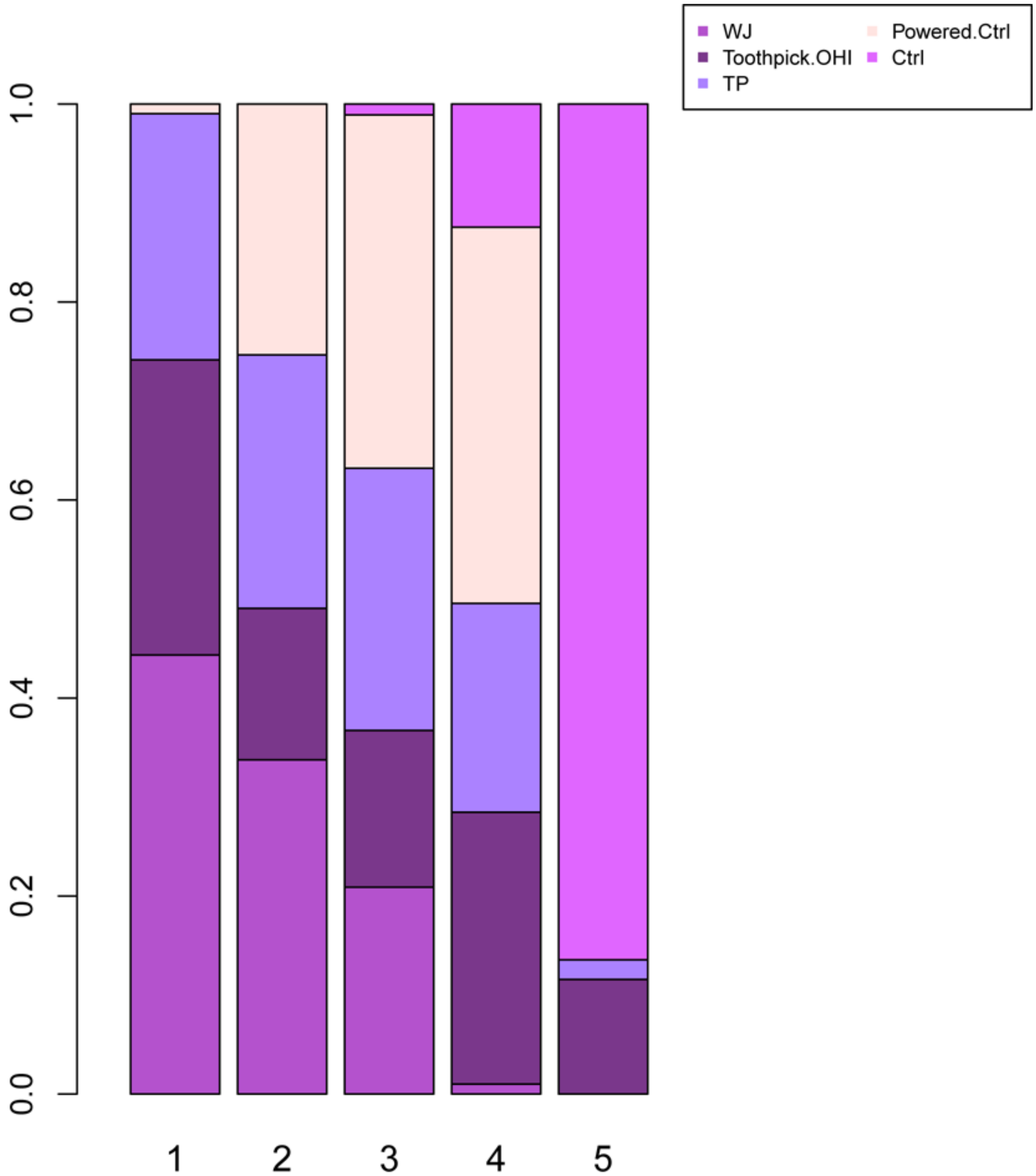
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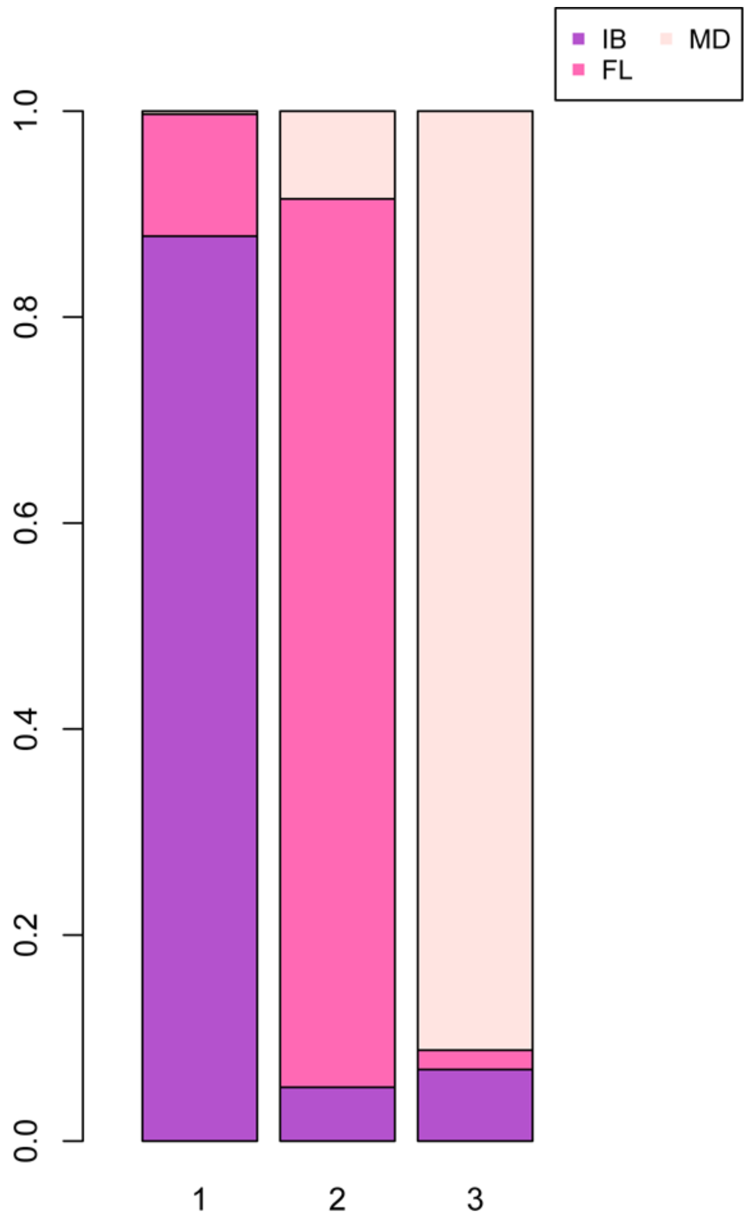

Figure 2.

Bar-plot of ranks for (a) BOP reduction, (b) GI reduction, (c) PCR reduction and (d) PD reduction

Table 1

Interdental OH interventions categories assessed in the present study

Group Name		Included OH methods ds
1	FL	Floss (waxed and unwaxed), flosser, super-floss
2	FL_2	Automated flosser and powered flossing devices
3	TP	Toothpick
4	TO	Toothpick and intensive Oral hygiene instructions
5	WJ	Water jet irrigation systems
6	IB	Interdental brushes
7	MD	Gum massaging devices
8	Ctrl	Toothbrush only controls
9	Powered Ctrl	Powered, electric, sonic toothbrush controls
10	PW	Powered control AND waterjet

Table 2

Study characteristics

First Author	Year	Design	Funding	Country	interdental OH method				Population	Follow-up
Walsh	1985	RCT	None reported	USA	Ctrl (N=12)	TP (N=12)	TO (N=12)		Healthy gingiva	24 weeks
Walsh	1989	RCT	Xouth Inc, PA, USA	USA	Ctrl (N=27)	Powered Ctrl (N=27)	WJ (N=27)	Powered Ctrl+WJ (N=27)	Gingivitis patients	24 weeks
Kazmierczak	1994	RCT	None reported	USA	MD (N=10)	FL (N=10)			Healthy gingiva	6 weeks
Gordon	1996	RCT	None reported	USA	FL_2 (N=30)	FL (N=30)			Healthy gingiva	4 weeks
Carter	1996	RCT	None	USA	FL (N=15)	FL (N=15)			NA	4 weeks
Isaacs	1999	RCT	Braun AG, Kronberg, Germany.	USA	FL_2 (N=73)	FL (N=72)			Gingivitis patients	24 weeks
Frascella	2000	RCT	None reported	Germany	Ctrl (N=30)	WJ (N=26)			Gingivitis patients	8 weeks
Shibly	2001	RCT	None reported	USA	WJ (N=35)	FL (N=35)			Healthy gingiva	4 weeks
Yankell	2002	RCT	None reported	USA	TP (N=32)	FL (N=31)			Healthy gingiva	4 weeks
Bauroth	2003	RCT	Pfizer Consumer Healthcare, Morris Plains, NJ	USA	FL (N=108)	Ctrl (N=110)			Gingivitis patients	24 weeks
Sharma	2004	RCT	Pfizer Consumer Healthcare, Pfizer, Morris Plains, NJ	Canada	Ctrl (N=81)	FL (N=81)			Gingivitis patients	24 weeks
Barnes	2005	RCT	None reported	USA	FL (N=35)	WJ (N=35)	Powered Ctrl+WJ (N=35)		Healthy gingiva	4 weeks
Cronin	2005	RCT	None reported	USA	FL (N=25)	TP (N=27)	FL_2 (N=26)		Gingivitis patients	4 weeks
Jared	2005	RCT	None reported	USA	IB (N=30)	FL (N=29)	Ctrl (N=32)		Healthy gingiva	4 weeks
Zimmer	2006	RCT	None reported	Germany	FL (N=39)	Ctrl (N=39)			Gingivitis patients	8 weeks
Schiff	2006	RCT	None reported	USA	FL (N=37)	Ctrl (N=37)	FL (N=40)		Gingivitis patients	24 weeks
Jackson	2006	RCT	Colgate-Palmolive	USA	FL (N=37)	IB (N=37)			Periodontitis patients	12 weeks
Biesbrock	2007	RCT	Procter & Gamble, Cincinnati, OH	USA	Ctrl (N=30)	Ctrl 2 (N=30)	Powered Ctrl (N=29)	FL_2 (N=28)	Healthy gingiva	8 weeks
Rosema	2011	RCT	None reported	Netherlands	WJ (N=34)	WJ (N=34)	FL (N=36)		Gingivitis patients	4 weeks
Goyal	2012	RCT	Waterpik, CO, USA	Canada	WJ (N=35)	Powered Ctrl (N=35)	Powered Ctrl (N=35)	Ctrl (N=35)	Gingivitis patients	4 weeks
Sharma	2012	RCT	Waterpik, CO, USA	Canada	WJ (N=41)	WJ (N=41)			Gingivitis patients	4 weeks
Mythri	2015	RCT	Colgate Palmolive India Ltd.	India	FL (N=40)	Ctrl (N=40)			Gingivitis patients	24 weeks

Table 3

Results of pairwise comparisons for reduction in gingival inflammation outcome measures (BOP, GI) based on NMA

	Floss	FL_2	TP	TO	WJ	IB	MD	Ctrl	Powered Ctrl
BOP	**Mean % BOP difference between OH methods (95% Confidence interval)**								
FL2	−0.011 (−0.049, 0.028)								
TP	0.016 (−0.033, −0.066)	0.027 (−0.027, 0.081)							
TO	0.187 (−0.002, 0.377)	0.198 (0.005, 0.391)	0.171 (−0.021, 0.362)						
WJ	0.116 (0.079, 0.153)	0.126 (0.073, 0.180)	0.099 (0.038, 0.160)	−0.072 (−0.263, 0.119)					
IB	0.071 (−0.054, 0.196)	0.082 (−0.049, 0.213)	0.054 (−0.080, 0.188)	−0.116 (−0.344, 0.11)	−0.045 (−0.175, 0.085)				
MD	−0.039 (−0.089, 0.011)	−0.028 (−0.091, 0.035)	−0.055 (−0.126, 0.014)	−0.226 (−0.422, −0.03)	−0.155 (−0.217, −0.093)	−0.110 (−0.244, 0.025)			
Ctrl	−0.077 (−0.103, −0.051)	−0.066 (−0.112, −0.020)	−0.094 (−0.149, −0.039)	−0.264 (−0.454, −0.075)	−0.193 (−0.224, −0.162)	−0.148 (−0.276, −0.020)	−0.038 (−0.094, 0.018)		
Powered Ctrl	0.013 (−0.026, 0.051)	0.024 (−0.031, 0.078)	−0.004 (−0.066, 0.058)	−0.175 (−0.366, 0.017)	−0.103 (−0.127, −0.079)	−0.058 (−0.189, 0.073)	0.052 (−0.011, 0.115)	0.09 (0.058, 0.121)	
PW	0.081 (−0.036, 0.199)	0.092 (−0.031, 0.215)	0.065 (−0.062, 0.192)	−0.106 (−0.328, 0.116)	−0.034 (−0.150, 0.083)	0.011 (−0.161, 0.182)	0.12 (−0.008, 0.248)	0.159 (0.041, 0.276)	

	Floss	FL_2	TP	WJ	IB	MD	Ctrl	Powered Ctrl
GI	**Mean GI difference between OH methods (95% Confidence interval)**							
FL_2	−0.044 (−0.081, −0.006)							
TP	−0.023 (−0.093, 0.048)	0.021 (−0.051, 0.093)						
WJ	0.104 (0.050, 0.158)	0.148 (0.096, 0.200)	0.127 (0.042, 0.212)					
IB	0.138 (0, 0.278)	0.182 (0.039, 0.325)	0.161 (0.005, 0.317)	0.034 (−0.115, 0.183)				
MD	0.07 (0.039, 0.102)	0.114 (0.065, 0.163)	0.093 (0.016, 0.170)	−0.034 (−0.097, 0.028)	−0.068 (−0.211, 0.074)			
Ctrl	−0.089 (−0.126, −0.053)	−0.046 (−0.066, −0.026)	−0.067 (−0.139, 0.006)	−0.194 (−0.244, −0.143)	−0.228 (−0.371, −0.086)	−0.16 (−0.208, −0.111)		

	Floss	FL_2	TP	WJ	IB	MD	Ctrl	Powered Ctrl
GI	**Mean GI difference between OH methods (95% Confidence interval)**							
Powered Ctrl	−0.024 (−0.063, 0.015)	0.02 (−0.003, 0.042)	−0.001 (−0.075, 0.072)	−0.128 (−0.179, −0.078)	−0.162 (−0.306, −0.02)	−0.094 (−0.144, −0.044)	0.065 (0.046, 0.085)	
PW	0.051 (−0.043, 0.146)	0.095 (−0.001, 0.191)	0.074 (−0.042, 0.190)	−0.053 (−0.145, 0.039)	−0.087 (−0.255, 0.081)	−0.019 (−0.119, 0.081)	0.141 (0.046, 0.236)	0.075 (−0.02, 0.172)

Table 4

Rank of each treatment for each outcome

BOP	**Mean Rank**	**SD**	**Prob(Best)***	**SUCRA**	**SUCRA_rank**
Toothpick+OHI	1.7	1.445	0.704	0.922	1
WJ	2.314	0.768	0.126	0.854	2
Powered Ctrl+WJ	3.48	1.787	0.089	0.724	3
IB	3.834	2.04	0.08	0.685	4
TP	5.515	1.419	0	0.498	5
Powered Ctrl	5.72	1.32	0	0.476	6
FL	6.583	0.977	0	0.38	7
FL_2	7.335	1.244	0	0.296	8
MD	8.631	1.002	0	0.152	9
Ctrl	9.889	0.325	0	0.012	10
GI	Mean Rank	SD	Prob(Best)*	SUCRA	SUCRA_rank
IB	1.734	1.241	0.647	0.908	1
WJ	1.948	0.74	0.274	0.882	2
MD	3.036	0.78	0.029	0.745	3
Powered Ctrl+WJ	3.709	1.399	0.049	0.661	4
FL	5.216	0.729	0	0.473	5
Powered Ctrl	6.358	0.76	0	0.33	6
TP	6.415	1.386	0	0.323	7
FL_2	7.623	0.559	0	0.172	8
Ctrl	8.96	0.196	0	0.005	9
PCR	Mean Rank	SD	Prob(Best)*	SUCRA	SUCRA_rank
IB	1.359	0.686	0.699	0.955	1
Powered Ctrl+WJ	2.342	1.767	0.293	0.832	2
MD	3.232	0.954	0.006	0.721	3
FL	4.833	1.022	0	0.521	4
WJ	5.206	1.883	0.001	0.474	5

BOP	**Mean Rank**	**SD**	**Prob(Best)***	**SUCRA**	**SUCRA_rank**
Powered Ctrl	5.661	1.073	0	0.417	6
TP	6.8	2.296	0.002	0.275	7
FL_2	7.221	0.8	0	0.222	8
PD	Mean Rank	SD	Prob(Best)*	SUCRA	SUCRA_rank
IB	1.191	0.542	0.878	0.904	1
FL	1.901	0.357	0.119	0.55	2
MD	2.908	0.299	0.003	0.046	3

* *Prob(Best):* Probability of being the best treatment

SUCRA: Surface under the cumulative ranking curve. The larger the SUCRA value for the treatment k, the higher its rank among the available treatment options. SUCRA would be 1 when a treatment is certain to be the best and 0 when a treatment is certain to be the worst