©Operative Dentistry, 2021, **46-5**, E199-E223

Evaluation of Tooth Sensitivity of In-office Bleaching with Different Light Activation Sources: A Systematic Review and a Network Meta-analysis

BM Moran • PK Ziegelmann • SB Berger • A Burey
T de Paris Matos • E Fernández • AD Loguercio • A Reis

Clinical Relevance

The use of light sources for in-office bleaching does not seem to exacerbate bleaching-induced tooth sensitivity.

SUMMARY

Objectives: A systematic review and network meta-analysis were performed to answer the following research question: Are there differences in the risk and the intensity of tooth sensitivity (TS) among eight light activation systems for in-office bleaching in adults?

Methods: Randomized controlled trials (RCTs) that compared at least two different in-office bleaching

*Bianca M Maran, DDS, MS, PhD, professor, Department of Restorative Dentistry, School of Dentistry, State University of Western Paraná, Cascavel, Paraná, Brazil; Postgraduate Program in Dentistry, School of Dentistry, University of North Paraná, Londrina, Paraná, Brazil

Patrícia K Ziegelmann, DDS, MS, PhD, associate professor, Statistics Department and Post-Graduation Program in Epidemiology, Federal University of Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil

Sandrine Bittencourt Berger DDS, MS, PhD, professor, Department of Restorative Dentistry, School of Dentistry, University of North Paraná, Londrina, Paraná,

Adrieli Burey, DDS, MS, PhD student, Department of Restorative Dentistry, School of Dentistry, State University of Ponta Grossa, Ponta Grossa, Paraná, Brazil

Thalita de Paris Matos, DDS, MS, PhD student, Department of Restorative Dentistry, School of Dentistry, State University of Ponta Grossa, Ponta Grossa, Paraná, Brazil

Eduardo Fernández, DDS, MS, PhD, professor, Department Restorative Dentistry, University of Chile, Santiago de Chile, Chile; Professor, Universidad Autónoma de Chile, Instituto de Investigaciones Biomédicas, Santiago de Chile Chile

Alessandro D Loguercio, DDS, MS, PhD, adjunct professor, Department of Restorative Dentistry, State University of Ponta Grossa, Ponta Grossa, PR, Brazil

Alessandra Reis, DDS, MS, PhD, adjunctive professor, Department of Restorative Dentistry, State University of Ponta Grossa, Ponta Grossa, PR, Brazil

*Corresponding author: Rua Engenharia, 464 – Universitário, Cascavel, Paraná, Brazil - 85819-190; e-mail: medeiros.bianca@hotmail.com

http://doi.org/10.2341/20-127-L

light activations were included. The risk of bias (RoB) was evaluated with the RoB tool version 1.0 from the Cochrane Collaboration tool. A random-effects Bayesian mixed treatment comparison (MTC) model was used independently for high- and low-concentration hydrogen peroxide. The certainty of the evidence was evaluated using the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) approach. A comprehensive search was performed in PubMed, Bridge Base Online (BBO), Latin American and Caribbean Health Sciences Literature database (LILACS), Cochrane Library, Scopus, Web of Science, and grey literature without date and language restrictions on April 23, 2017 (updated on September 26, 2019). Dissertations and theses, unpublished and ongoing trials registries, and IADR (International Association for Dental Research) abstracts (2001–2019) were also searched.

Results: After title and abstract screening and the removal of duplicates, 32 studies remained. Six were considered to be at low RoB, three had high RoB, and the remaining had an unclear RoB. The MTC analysis showed no significant differences among the treatments in each network. In general, the certainty of the evidence was graded as low due to unclear RoB and imprecision.

Conclusion: There is no evidence that the risk and intensity of TS are affected by light activation during in-office bleaching.

INTRODUCTION

A Brazilian study[1] that evaluated patients' desire to undergo dental bleaching reported that 85.9% of the patients wanted to undertake the treatment, and this desire was 2.31 times higher in patients who visited the dentist in the last year, compared to those who visited the dentist more than a year ago. Another cross-sectional study conducted in Iran[2] reported that approximately 62% of patients preferred dental bleaching for cosmetic treatment. In Israel,[3] a study showed that 56.2% of patients were not happy with the color of their teeth and that dental bleaching was the treatment most desired by patients. Therefore, dental bleaching has become the treatment of choice to improve patients' smiles and self-esteem[4] because it is a simple and non-invasive technique for the treatment of discolored teeth.

Currently, there are three types of dentist-supervised bleaching techniques: at-home bleaching, in-office bleaching, and combined bleaching technique.[5,6] Regardless of the bleaching technique, the mechanism of action seems to be the oxidization of organic components of the dental substrate by unstable free radicals produced by the dissociation of hydrogen peroxide (HP), an oxidizing agent capable of diffusing into the dental structure.[7]

Although at-home bleaching is widely used by patients,[8] in-office bleaching is usually chosen by patients who do not like wearing trays and who wish for more immediate results.[9] There are various bleaching agent brands that vary in concentration,[10] pH,[11] application method,[12] and duration of application,[13] factors which may play a role in the degree of whitening. Additionally, bleaching agents can be used with light sources,[14] with the aim of accelerating the bleaching effect. Light-emitting diodes (LEDs), lasers, halogen lamps, and plasma arc lamps (PACs) are some of the devices used for light activation of the bleaching gel.

It is known that different light activation systems vary in type of lamp, energy outcome, energy delivery, and generated heat. For instance, the heat produced by a PAC is much higher than that produced by a halogen lamp,[15] which, in turn, is higher than that produced by an LED.[16] Although we have shown in previous network analysis that these differences had no impact on the whitening outcome,[17] they may affect patient experiences of tooth sensitivity (TS).

The systematic review of the literature with network meta-analysis performed in this work allows the comparison of different treatments in a single model and provides clinicians with scientific evidence on the effectiveness of multiple interventions.[18] Mixed treatment comparison (MTC) models combine two sources of evidence: the indirect one that comes from different trials with a common comparator (such as bleaching without light) and direct comparisons of light activation (that is, head-to-head trials).[19]

Thus, the purpose of this systematic review was to compare the risk and intensity of bleaching-induced TS associated with different light sources: light-free and seven types of light-activated bleaching (halogen lamp, laser, LED/laser, LED, metal halide light, violet light, and PAC) for high- or low-concentration HP.

METHODS AND MATERIALS

Protocol and Registration

This study protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO) under number CRD42018095806 and followed the recommendations of the Preferred

Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for reports.[20]

Eligibility Criteria

The following participant-intervention-comparator-outcome (PICO) framework research question was investigated in this study: Are there differences in the risk and intensity of tooth sensitivity associated with in-office bleaching performed in adults with eight different light activation systems (light-free, halogen lamp, LED/laser, LED, metal halide light, violet light, laser, and PAC)?

We included parallel and split-mouth RCTs that compared at least two of these different light activation systems. RCTs were excluded if they compared in-office dental bleaching with combined bleaching. To minimize publication bias, no year or language restrictions were applied.

Information Sources and Search Strategy

Controlled vocabulary (MeSH terms) and free keywords, defined based on the concepts of the PICO question, were used for the search strategy. The search strategy was first performed in MEDLINE (Table 1) via PubMed and then adapted to other databases (Cochrane Library, Brazilian Library in Dentistry, LILACS, and the citation databases Scopus and Web of Science) (Table 1). The reference lists of all primary studies were hand-searched for additional relevant publications. We also searched the first page of related article links of each primary study in the PubMed database to increase the sensitivity of the search.

Additionally, grey literature was investigated by searching dissertations and theses from the ProQuest Dissertations and Theses full-text database, Periódicos Capes Theses database, the abstracts of the annual conference of the International Association for Dental Research and its regional divisions (2001-2019), and the database System for Information on Grey Literature in Europe. The following clinical trial registries were also inspected to locate unpublished and ongoing trials: Current Controlled Trials, International Clinical Trials Registry Platform, ClinicalTrials.gov, ReBEC, and EU Clinical Trials Register.

Study Selection and Data Collection Process

Articles that appeared in more than one database were considered only once. After removal of duplicates, three review authors (BMM, AB, and TPM) screened the articles by title and then by abstract. When the title and abstract presented insufficient information, full-text articles were obtained to make a clear decision. Subsequently, the three reviewers classified those that met the inclusion criteria.

Each eligible article received a study ID combining the first author's name and the year of publication. Relevant information about the study design, participants, interventions, and outcomes was extracted independently, using customized extraction forms. In the case of disagreements between the review authors, a fourth author was consulted (AR). Studies usually assess TS at different points in time, which is a source of variation among them; to deal with that problem, we collected the worst mean/score value from the numeric rating scale (NRS) or visual analog scale (VAS) for the risk and intensity of TS reported for the study group.

In studies with more than two experimental groups (ie, three- or four-arm studies), different pairwise comparisons were included in the network meta-analysis. However, to avoid double counts of the "shared group," the number of events and participants was divided approximately evenly between comparisons for dichotomous outcomes. For continuous outcomes, the means and standard deviations were kept constant, and the number of patients divided among the comparisons.

Risk of Bias in Individual Studies

The risk of bias (RoB) of the eligible trials was determined by three independent reviewers using the RoB tool from the Cochrane Collaboration for RCTs.[21] The assessment criteria are composed of six domains: selection bias (adequate sequence generation and allocation concealment), performance bias (blinding of participants and patients), detection bias (blinding of evaluators), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other sources of bias. The last domain was not assessed in this systematic review. Disagreements between the reviewers were solved through discussion and, if needed, by consulting a fourth reviewer (AR).

Each domain level was judged as low, high, or unclear RoB. At the study level, the study was considered to have low RoB if all domains of each outcome had low RoB. If one or two key domains were judged as having unclear RoB, the study was classified as unclear RoB; if at least one key domain had high RoB, the study was considered to have high RoB.

Summary Measures and Statistical Analyses

Independent analyses were performed for two outcomes (intensity of TS with pain scales, risk of TS) and considered both high- and low-concentration bleaching gels. Products with HP concentrations higher than 25% were classified as high-concentration

Table 1: *Electronic Database and Search Strategy Conducted Initially on April 23, 2017 (updated on September 26, 2019)*

PUBMED (#1 and #2 and #3)		
#1 ((((((((((((((((((((tooth discoloration[MeSH Terms]) OR dentition, permanent[MeSH Terms]) OR color[MeSH Terms]) OR color[Title/Abstract]) OR colour[Title/Abstract]) OR "tooth discoloration"[Title/Abstract]) OR "tooth discolouration"[Title/Abstract]) OR "teeth discoloration"[Title/Abstract]) OR "teeth discolouration"[Title/Abstract]) OR "discolored tooth"[Title/Abstract]) OR "discolored teeth"[Title/Abstract]) OR "discoloured tooth"[Title/Abstract]) OR "discoloured teeth"[Title/Abstract]) OR "tooth staining"[Title/Abstract]) OR "teeth staining"[Title/Abstract]) OR "dental discoloration"[Title/Abstract]) OR "dental discolouration"[Title/Abstract]) OR "stained teeth"[Title/Abstract]) OR "stained tooth"[Title/Abstract]) OR "dental staining"[Title/Abstract]	#2 ((((((((((((((((((tooth bleaching[MeSH Terms]) OR peroxides[MeSH Terms]) OR tooth bleaching agents[MeSH Terms]) OR hydrogen peroxide[MeSH Terms]) OR carbamide peroxide[Supplementary Concept]) OR light[MeSH Terms]) OR lasers[MeSH Terms]) OR bleaching[Title/Abstract]) OR whitening[Title/Abstract]) OR "hydrogen peroxide"[Title/Abstract]) OR "carbamide peroxide"[Title/Abstract]) OR "in office"[Title/Abstract]) OR "light activation"[Title/Abstract]) OR heat[Title/Abstract]) OR ultraviolet[Title/Abstract]) OR lamp[Title/Abstract]) OR "light activated"[Title/Abstract]) OR LED[Title/Abstract]	#3 (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR ("clinical trial"[tw]) OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR (placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR comparative study[pt] OR evaluation studies as topic[mh] OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospective*[tw] OR volunteer*[tw]) NOT (animals[mh] NOT humans[mh])
COCHRANE (#8 and #15)		
#1 MeSH descriptor: [Tooth Discoloration] explode all trees #2 MeSH descriptor: [Dentition, Permanent] explode all trees #3 MeSH descriptor: [Color] explode all trees #4 t*th next discoloration:ti,ab,kw or discolored next t*th:ti,ab,kw or t*th next staining:ti,ab,kw or dental next discoloration:ti,ab,kw or stained next t*th:ti,ab,kw (Word variations have been searched) #5 dental next staining:ti,ab,kw or color:ti,ab,kw (Word variations have been searched) #6 #1 or #2 or #3 or #4 or #5 #7 MeSH descriptor: [Tooth Bleaching] explode all trees #8 MeSH descriptor: [Peroxides] explode all trees	#9 MeSH descriptor: [Tooth Bleaching Agents] explode all trees #10 MeSH descriptor: [Hydrogen Peroxide] explode all trees #11 MeSH descriptor: [Light] explode all trees #12 MeSH descriptor: [Lasers] explode all trees #13 "carbamide peroxide":ti,ab,kw or bleaching:ti,ab,kw or whitening:ti,ab,kw or "hydrogen peroxide":ti,ab,kw or "in office":ti,ab,kw (Word variations have been searched) #14 light next activat*:ti,ab,kw or heat:ti,ab,kw or ultraviolet:ti,ab,kw or lamp:ti,ab,kw or LED:ti,ab,kw (Word variations have been searched) #15 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14	

Table 1: *Electronic Database and Search Strategy Conducted Initially on April 23, 2017 (updated on September 26, 2019) (Continued)*

LILACS/BBO (#1 and #2)	
#1 (MH:"tooth discoloration" OR MH:"dentition permanent" OR MH:color OR color OR cor OR colour OR "tooth discolouration" OR "descoloração de dente" OR "decoloración de lo diente" OR "teeth discoloration" OR "decoloración de los dientes" OR "descoloração dos dentes" OR "teeth discolouration" OR "discolored tooth" OR "diente descolorido" OR "dente descolorido" OR "discolored teeth" OR "dientes descoloridos" OR "dentes descoloridos" OR "discoloured tooth" OR "discoloured teeth" OR "tooth staining" OR "manchas en los dientes" OR "manchamento dental" OR "dental discoloration" OR "decoloración dental" OR "descoloração dental" OR "dental discolouration" OR "stained teeth" OR "dientes manchados" OR "dentes manchados" OR "stained tooth" OR "diente manchado" OR "dente manchado" OR "dental staining" OR "mancha en los dientes" OR "mancha nos dentes")	#2 (MH:"tooth bleaching" OR MH:peroxides OR MH:"tooth bleaching agents" OR MH:"hydrogen peroxide" OR MH:light OR MH:lasers OR "peroxide carbamide" OR "peróxido de carbamida" OR bleaching OR blanqueo OR branqueamento OR whitening OR blanqueamiento OR "in office" OR "en el consultorio" OR "em consultório" OR "light activation" OR "activación de la luz" OR fotoativação OR heat OR calor OR ultraviolet OR ultravioleta OR lamp OR lámpara OR lâmpada OR "light activated" OR "activado por la luz" OR "ativado por luz" OR LED)
SCOPUS (#1 and #2)	
#1 (TITLE-ABS-KEY ("permanent dentition") OR TITLE-ABS-KEY ("t??th discoloration") OR TITLE-ABS-KEY (colo*r) OR TITLE-ABS-KEY ("t??th discolouration") OR TITLE-ABS-KEY ("discoloured t??th") OR TITLE-ABS-KEY ("discolored t??th") OR TITLE-ABS-KEY ("t??th staining") OR TITLE-ABS-KEY ("dental discolo*ration") OR TITLE-ABS-KEY ("stained t??th") OR TITLE-ABS-KEY ("dental staining"))	#2 TITLE-ABS-KEY ("t??th bleaching") OR TITLE-ABS-KEY (peroxides) OR TITLE-ABS-KEY ("t??th bleaching agents") OR TITLE-ABS-KEY ("hydrogen peroxide") OR TITLE-ABS-KEY (light) OR TITLE-ABS-KEY (lasers) OR TITLE-ABS-KEY (bleaching) OR TITLE-ABS-KEY (whitening) OR TITLE-ABS-KEY ("carbamide peroxide") OR TITLE-ABS-KEY ("in office") OR TITLE-ABS-KEY ("light activat*") OR TITLE-ABS-KEY (heat) OR TITLE-ABS-KEY (ultraviolet) OR TITLE-ABS-KEY (lamp) OR TITLE-ABS-KEY (led)
WEB OF SCIENCE (#1 and #2)	
#1 Tópico: ("permanent dentition") OR Tópico: ("t*th discolo*ration") OR Tópico: (colo$r) OR Tópico: ("discolo*red t*th") OR Tópico: ("t*th staining") OR Tópico: ("dental discolo*ration") OR Tópico: ("stained t*th") OR Tópico: ("dental staining")	#2 Tópico: ("t*th bleaching") OR Tópico: (peroxides) OR Tópico: ("tooth bleaching agents") OR Tópico: ("hydrogen peroxide") OR Tópico: (light) OR Tópico: (lasers) OR Tópico: (bleaching) OR Tópico: (whitening) OR Tópico: ("carbamide peroxide") OR Tópico: ("in office") OR Tópico: ("light activat*") OR Tópico: (heat) OR Tópico: (ultraviolet) OR Tópico: (lamp) OR Tópico: (LED)

products, and those with concentrations equal to or lower than 25% were considered low-concentration products. This classification was done based on the previous knowledge of the different HP concentrations available in the international dental market. Although this arbitrary classification may have implications in the study results, lack of classification would merge a wide variety of HP concentrations into a single group, providing unrealistic findings.

Traditional and network meta-analyses were conducted using mean difference (MD) or standardized mean difference (SMD) for the intensity of TS and risk ratio (RR) for risk of TS. The choice of the effect measure for continuous outcomes depended on whether or not studies used different instruments/scales for measurement of the outcome. For the intensity of TS, we included in the meta-analyses studies that used VAS or NRS scales, and SMD was chosen as the effect measure.

Traditional meta-analysis was performed for all pairwise comparisons where evidence was available from one or more head-to-head studies. Random effect models with the DerSimonian and Laird variance estimator were used since high heterogeneity among studies was expected. The Mantel-Haenzel method was used for the risk of TS (dichotomous), and the inverse of the variance method was used for the intensity of TS (continuous). The I^2 statistic and the Cochran Q test were used to measure heterogeneity among studies.

MTC is a Bayesian hierarchy model supported by Markov Chain Monte Carlo (MCMC) methods. Its versatility allows the simultaneous comparison of all eight treatments and the incorporation of trials with three or more arms. The evidence of each possible pairwise comparison was evaluated exclusively from direct evidence (head-to-head trials), exclusively from indirect evidence (trials with a common comparator), or from a combination of both, depending on what evidence was available for each pair. Both fixed and random effects with homogeneity of variances were adjusted, and the one with the better performance following the Deviance Information Criterion (DIC) was chosen. The consistency assumption was checked for all pairwise comparisons that had both direct and indirect evidence, using the Bayesian *p*-values produced by the node-splitting method proposed by Dias and others.[22] The evidence of a pair was considered inconsistent if the *p*-value was lower than the significance level (α=0.05) adjusted for multiple comparisons. The results were displayed in point estimates and 95% credible intervals (CrIs, [CrIs are the Bayesian equivalent of frequentist confidence intervals]). Surface under the cumulative ranking curve (SUCRA) values (higher values indicate smaller risk or intensity of TS) were also calculated if at least one comparison of the network was found to have a significant difference. All analyses were implemented using the meta (multi-environment trail analysis) and GeMTC packages of the R statistical program (R Foundation).

Assessment of the Certainty of the Evidence Using Grading of Recommendations: Assessment, Development, and Evaluation

We followed the GRADE approach to appraise the confidence in estimates derived from network meta-analysis. Direct evidence from RCTs starts at high confidence and can be rated down based on RoB, indirectness, imprecision, or inconsistency (heterogeneity); publication bias can be rated to levels of moderate, low, and very low confidence. The rating of indirect estimates starts at the lowest rating of the pairwise estimates that contribute as first-order loops to the indirect estimate but can be rated down further due to imprecision or intransitivity (dissimilarity between studies in terms of clinical or methodological characteristics). If direct and indirect estimates are similar (ie, coherent), then the higher of their ratings can be assigned to the network meta-analysis estimates.

RESULTS

Study Selection

The database screening returned a total of 9442 studies, which was reduced to 5541 following the removal of duplicates. After title screening, 227 studies remained, and this number was reduced to 32 full texts that were assessed for eligibility (Figure 1).

Characteristics of Included Articles

Study Design and Method of Tooth Sensitivity Evaluation—

The characteristics of the 32 eligible primary studies are listed in Table 2. The study design was balanced: nineteen studies used parallel design[14,23-41] and thirteen studies used the split-mouth design.[42-54]

Twenty studies evaluated the intensity of TS; of these, fourteen employed the VAS for pain evaluation,[a] five employed the NRS,[24,27,29,42,45] and only one[36] employed both the VAS and NRS.

The risk of TS was evaluated in twelve studies.[b]

[a] Ref. 23,25,26,30,34,35,38,40,43,46,48-50,54,55.

[b] Ref. 14,23,25-29,31-33,36,39,41,42,44,45,47,48,52,53.

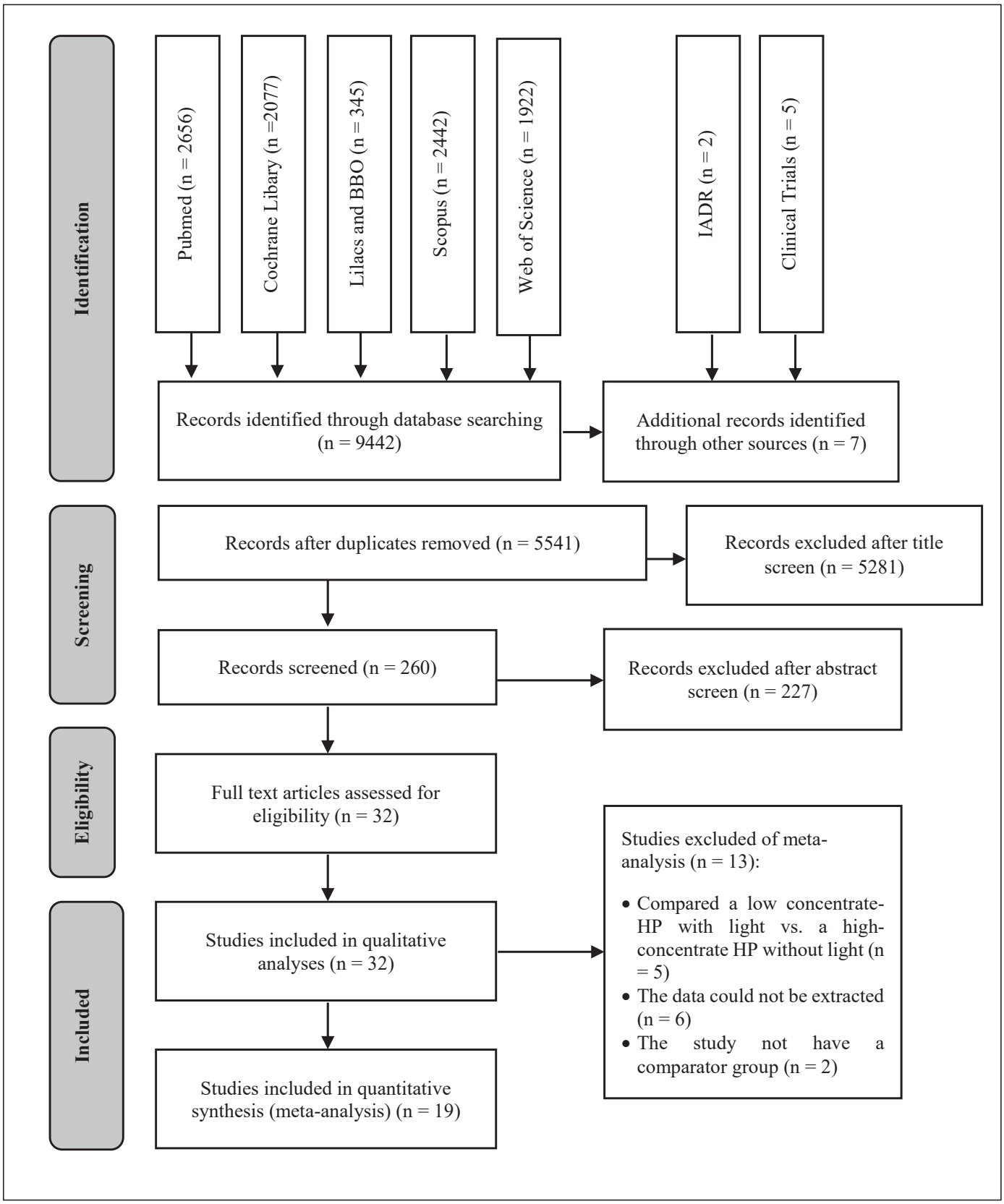

Figure 1. *Flow diagram of study identification.*

Table 2: *Summary of the Primary Studies Included in this Systematic Review*

Study ID	Study Design [setting]	Subjects' Age, Mean ± SD [range] (y)	Number of Subjects [%] (male)	Baseline Color/ Evaluated Tooth	Groups and Materials/Number of Patients per Group
Almeida, 2012[23]†	Parallel [n.r.]	n.r. ± n.r. [18-28]	n.r. [n.r.]	n.r./n.r.	I: AH 10% CP^{a}/10 II: IO 35% HP^{bLF}/10 III: IO 35% HP^{b} + light^{HL}/10 IV: IO 35% HP^{b} + light^{LL}/10
Almeida Farhat, 2014[42]	Split-mouth [n.r.]	n.r ± n.r. [18-30]	n.r. [n.r.]	C_2/Anterior teeth	I: IO 35% HP^{c} + light^{LED}/16 II: IO 35% HP^{c} + light^{LL}/16
Alomari, 2010[24]†	Parallel [n.r.]	27.8 ± n.r. [18-40]	12 [30.0]	A_3/Anterior teeth	I: IO 35% HP^{dLF}/10 II: IO 35% HP^{d} + light^{HL}/10 III: IO 35% HP^{d} + light^{LED}/10 IV: IO 35% HP^{d} + light^{MHL}/10
Bernardon, 2010[43]	Split-mouth [n.r.]	n.r. ± n.r. [n.r.-n.r.]	n.r. [n.r.]	A_2/Anterior teeth	I: AH 10% CP^{a} vs. IO 35% HP^{b} + light^{LL}/30 II: IO 35% HP^{bLF} vs. IO 35% HP^{b} + light^{LL}/30 III: AH 10% CP^{a} vs. IO 35% HP^{b} + light^{LL} [1 session] and AH 10% CP^{a}/30
Bortolatto, 2013[25]	Parallel [n.r.]	n.r. ± n.r. [18-25]	n.r. [n.r.]	n.r./n.r.	I: IO 35% HP^{cLF}/20 II: IO 35% HP^{c} + light^{LL}/20
Bortolatto, 2014[26]	Parallel [University]	21.1 ± 2.26 [18-25]	n.r. [n.r.]	n.r./Anterior teeth	I: IO 15% HP^{e} + light^{LL}/20 II: IO 35% HP^{cLF}/20
Bortolatto, 2016[27]	Parallel [University]	24.15 ± 3.92 [18-25]	24 [50]	n.r./n.r.	I: IO 6% HP^{e} + light^{LL}/24 II: IO 35% HP^{f} + light^{LL}/24
Brugnera 2019[28]	Parallel [University]	27.6 ± 4.70 [20-35]	11 [22.0]	A_2/Canine	I: IO 35% CP^{gLF}/25 II: IO 35% CP^{g} + light^{VL}/25

Table 2: *Summary of the Primary Studies Included in this Systematic Review (Extended)*

Bleaching Protocol	**Light Source**			
Applications x min [sessions] – interval (days)	**Light Protocol: Applications x time (interval)**	**Spectrum (nm) / Intensity, (mW/cm²) / Power output (W)**	**Tooth Sensitivity Scale [outcome]**	**Follow-up [Drop-outs]**
I: 4h/daily (21 days) II-IV: 3 x 10 [3] – 7	III: 3 x 20 sec (n.r.) IV: 3 x 3 min (n.r.)	III: 450-500 / 400 / n.r. IV: 470 and 808 / 120 and n.r. / n.r. and 0.2	VAS 0-10 [Risk and Intensity of TS]	During [0] Immediately [0] 7 d [0] 30 d [0] 180 d [0]
I-II: 3 x 10 [2] – 7	I-II: 3 x 1 min (2-min)	I: n.r. / n.r. / n.r. II: 425-480 and 810 / 300 and 300 / 0.3 and 0.2	NRS 0-4 [Risk and Intensity of TS]	During Immediately [0] 12 h [0] 1 d [0] 2 d [0] 30 d [0] 180 d [0]
I-IV: 3 x 20 [1]	II-IV: 3 x 20 min (0-min)	II-IV: n.r./ n.r. / n.r.	NRS 0-3 [Intensity of TS]	Immediately [n.r.] 30 d [n.r.]
AH: 8h/daily (14 days) IO: 3 x 15 [2] – 15	I-III: 1 x 4 min (n.r.)	I-III: n.r. and n.r. / n.r. / n.r. and n.r.	VAS 0-10 [Intensity of TS]	Daily [n.r.]
I: 3 x 15 [3] – 7 II: 3 x 8 [3] – 7	I-II: 4 x 1 min (n.r.)	II: 425-480 and 810 / 300 and 300 / 1.8 and 0.6	VAS 0-100 [Risk and Intensity of TS]	Immediately [8]
I: 3 x 16 [3] – 7 II: 3 x 15 [3] – 7	I: 4 x 1 min (2-min)	I: 455-485 and 808 / 300 and 300 / 1.8 and 0.6	VAS 0-100 [Risk and Intensity of TS]	7 d [15] 14 d [15] 21 d [15]
I-II: 2 x 12 [2] – 7	I-II: 6 x 1 min (1-min)	I-II: 455-485 and 810 / 300 and 300 / 1.8 and 0.6	NRS 0-3 [Risk and Intensity of TS]	Immediately [0] 7 d [0] 14 d[0]
I-II: 1 x 30 [2] – 7	II: 20 x 1 min (30-sec)	II: 405-410 / 300 / 1.2	VAS 0-100 [Risk of TS]	Immediately [0] 7 d [0] 14 d [0]

Table 2: *Summary of the Primary Studies Included in this Systematic Review (Continued)*

Study ID	Study Design [setting]	Subjects' Age, Mean ± SD [range] (y)	Number of Subjects [%] (male)	Baseline Color/ Evaluated Tooth	Groups and Materials/Number of Patients per Group
Ferraz 2018[29]	Parallel [University]	26.4 ± n.r. [18-40]	21 [38.9]	A_1/n.r.	I: 6% HP^e + $light^{LL}$/27 II: 15% HP^e + $light^{LL}$/27
Freitas, 2016[44]	Split-mouth [University]	20.5 ± n.r. [18-25]	10 [45.4]	A_2/Anterior teeth	I: IO 35% HP^{cLF}/22 II: IO 35% HP^c + $light^{LL}$/22
Gomes, 2008[45]	Split-mouth [n.r.]	n.r. ± n.r. [20-30]	n.r. [n.r.]	n.r./n.r.	I: IO 35% HP^b + $light^{LED}$ vs. IO 35% HP^b + $light^{HL}$/12 II: IO 35% HP^b + $light^{LL}$ vs. IO 35% HP^{bLF}/12
Gurgan, 2010[30]†	Parallel [n.r.]	27.3 ± n.r. [18-30]	11 [27.5]	A_3/Anterior teeth	I: IO 38% HP^{dLF}/10 II: IO 37% HP^h + $light^{LA}$/10 III: IO 35% HP^i + $light^{PAC}$/10 IV: IO 38% HP^j + $light^{LED}$/10
Henry, 2013[46]	Split-mouth [n.r.]	38.4 ± 13.64 [n.r.-n.r.]	24 [49.0]	A_3/Anterior teeth	I: IO 25% HP^k + $light^{MHL}$/49 II: IO 25% HP^{kLF}/49
Kossatz, 2011[31]	Parallel [University]	n.r. ± n.r. [n.r-n.r.]	n.r. [n.r.]	C_2/Upper central incisors	I: IO 35% HP^b + $light^{LL}$/15 II: IO 35% HP^{bLF}/15
Kugel, 2006[47]	Split-mouth [n.r.]	n.r. ± n.r. [n.r.-n.r.]	n.r. [n.r.]	A_3/Anterior teeth	I: IO 15% HP^l + $light^{MHL}$/10 II: IO 38% HP^{dLF}/10
Kugel, 2009[32]	Parallel [University]	30.9 ± n.r. [22-48]	n.r. [n.r.]	A_2/n.r.	I: IO 25% HP^m + $light^{MHL}$/11 II: IO 25% HP^{mLF}/11 III: $Light^{MHL}$/11
Marson, 2008[33]†	Parallel [n.r.]	n.r. ± n.r. [18-28]	n.r. [n.r.]	n.r./Anterior teeth	I: IO 35% HP^{bLF}/10 II: IO 35% HP^b + $light^{HL}$/10 III: IO 35% HP^b + $light^{LED}$/10 IV: IO 35% HP^b + $light^{LL}$/10

Table 2: *Summary of the Primary Studies Included in this Systematic Review (Extended)*

Bleaching Protocol	**Light Source**			
Applications x min [sessions] – interval (days)	**Light Protocol: Applications x time (interval)**	**Spectrum (nm) / Intensity, (mW/cm²) / Power output (W)**	**Tooth Sensitivity Scale [outcome]**	**Follow-up [Drop-outs]**
I-II: 3 x 10 [3] – 7	I-II: 5 x 1 min (n.r.)	I-II: 470 and 808/ 300 and 300 / 1.8 and 0.6	NRS 0-3 [Risk and Intensity of TS]	7 d [2] 14 d [2] 30 d [2]
I: 3 x 15 [1] II: 3 x 8 [1]	II: 3 x 1 min (n.r.)	470 and 810 / 350-400 and n.r. / n.r. and 0.2	VAS 0-10 [Risk of TS]	Immediately [0] 1 d [0]
I-II: 3 x 15 [2] – 7	I: 3 x 30 sec (n.r.) II: 3 x 3 min (n.r.)	I: 440-480 vs. n.r. / 1400 vs. n.r. / n.r. vs. n.r. II: 470 and 830 / 500 and 5036 / n.r. and n.r.	NRS 0-3 [Risk and Intensity of TS]	During [0] Immediately [0]
I: 2 x 15 [1] II: 3 x 8 [1] III: 3 x 20 [1] IV: 2 x 20 [1]	II: 8 x 15 sec (1-min) III: 3 x 10 min (30-sec) IV: 2 x 20 min (0-min)	II: 815 / n.r. / 10 III: 400-490 / 2800 / n.r IV: 400-500 / n.r. / n.r.	VAS 0-10 [Intensity of TS]	Immediately [0]
I-II: 3 x 15 [1]	I: 3 x 15 min (0-min)	I: n.r. / n.r. / n.r.	VAS 0-100 [Intensity of TS]	Immediately [0] 7 d [0] 14 d [0]
I-II: 3 x 15 [2] – 7	I: 5 x 1 min (2-min)	I: 470 and 830 / 200 and n.r. / n.r. and n.r.	NRS 0-4 [Risk of TS]	Immediately [0] 1 d [0] 2 d [0]
I-II: 3 x 20 [1]	I: 3 x 20 min (0-min)	n.r. / n.r. / n.r.	Questionnaire [Risk of TS]	14 d [0]
I-III: 3 x 20 [1]	I and III: 3 x 20 min (0-min)	n.r. / n.r. / n.r.	NRS 0-3 [Risk of TS]	Immediately [0] 7 d [0] 30 d [3]
I-IV: 3 x 15 [2] – 7	II-IV: 3 x 15 min (0-min)	II: 400-500 / n.r./ n.r. III: 450-500 / n.r. / n.r. IV: 470 and n.r. / n.r. and n.r. / n.r. and n.r.	NRS 1-4 [Risk of TS]	During [0]

Table 2: *Summary of the Primary Studies Included in this Systematic Review (Continued)*

Study ID	Study Design [setting]	Subjects' Age, Mean ± SD [range] (y)	Number of Subjects [%] (male)	Baseline Color/ Evaluated Tooth	Groups and Materials/Number of Patients per Group
Martin, 2013[34]; Moncada, 2013[38]	Parallel [University]	23.0 ± 3.77 [18-37]	23 [26.1]	n.r./n.r.	I: IO 15% HP^{e} + light^{LL}/25 II: IO 35% HP^{c} + light^{LL}/27 III: IO 35% HP^{nLF}/36
Martin, 2015[35]	Parallel [University]	23.6 ± 4.00 [18-37]	n.r. [n.r.]	n.r./n.r.	I: IO 15% HP^{e} + light^{LL}/35 II: IO 35% HP^{c} + light^{LL}/35
Martín, 2015[48]	Split-mouth [n.r.]	24.5 ± 6.33 [18-44]	19 [63.3]	A_2/Central incisors	I: IO 35% HP^{c} + light^{LL}/30 II: IO 6% HP^{c} + light^{LL}/30
Mena Serrano, 2016[36]	Parallel [University]	22.5 ± 3.81 [18-27]	27 [35.1]	A_3/Upper Canine	I: IO 20% HP^{bLF}/19 II: IO 20% HP^{b} + light^{LL}/19 III: IO 35% HP^{bLF}/20 IV: IO 35% HP^{b} + light^{LL}/19
Michielin 2015[37]	Parallel [n.r.]	n.r. ± n.r. [n.r.-n.r.]	n.r. [n.r.]	n.r./n.r.	I: IO 10% HP$^{n.r.}$ + light^{VL}/12 II: IO 15% HP^{e} + light^{LL}/12 III: IO 35% HP^{f} + light$^{n.r.}$/12 IV: 35% HP^{fLF}/12
Mondelli, 2012[49]	Split-mouth [n.r.]	n.r. ± n.r. [n.r.-n.r.]	n.r. [n.r.]	A_3/Anterior teeth	I: IO 35% HP^{c} + light^{LL} vs. II: IO 35% HP^{cLF}/16 III: IO 38% HP^{d} + light^{LL} vs. IV: IO 38% HP^{dLF}/16 IV: AH 15% CP^{o}/16
Mondelli 2018[50]	Split-mouth [n.r.]	n.r. ± n.r. [n.r.-n.r.]	n.r. [n.r.]	A_3/Anterior teeth	I: IO 35% HP^{c} + light^{LL} vs. II: IO 35% HP^{cLF}/10 III: IO 35% HP^{b} + light^{LL} vs. IV: IO 25% HP^{cLF}/10
Ontiveros, 2009[51]	Split-mouth [n.r.]	n.r. ± n.r. [n.r.-n.r.]	n.r. [n.r.]	A_2/Anterior teeth	I: IO 25% HP^{k} + light^{MHL}/20 II: IO 25% HP^{kLF}/20

Table 2: *Summary of the Primary Studies Included in this Systematic Review (Extended)*

Bleaching Protocol	**Light Source**			
Applications x min [sessions] – interval (days)	**Light Protocol: Applications x time (interval)**	**Spectrum (nm) / Intensity, (mW/cm²) / Power output (W)**	**Tooth Sensitivity Scale [outcome]**	**Follow-up [Drop-outs]**
I: 3 x 15 [1] II: 3 x 10 [1] III: 1 x 45 [1]	I: 5 x 1 and 30 sec (n.r.) II: 5 x 1 min (1-min)	I-II: 450 and 830 / 400 and 100 / 1.8 and 0.4	VAS 0-100 [Intensity of TS]	Immediately [0] 7 d [27] 30 d [46]
I: 3 x 15 [1] II: 3 x 12 [1]	I: 3 x 15 min (0-min) II: 3 x 12 min (0-min)	I-II: 450 and 808 / 400 and 100 / n.r. and n.r.	VAS 0-100 [Intensity of TS]	Immediately [0] 7 d [16] 30 d [20]
I-II: 2 x 12 [3] – 7	I-II: 2 x 12 min (0-min)	I-II: n.r and n.r. / n.r. and n.r. / n.r. and 1.5	VAS 0-100 [Risk and Intensity of TS]	Immediately [0] 7 d [1] 14 d [1]
I-IV: 3 x 15 [2] – 7	5 x 1 min (2-min)	II and IV: 470 and 830 / 200 and 200 / n.r. and n.r.	VAS 0-10 NRS 0-4 [Risk and Intensity of TS]	During [0] Immediately [0] 2 d [0]
I-II: 5 x 7,5 [n.r.] – 7 III: 3 x 7,5 [n.r.] – 7 IV: 3 x 15 [n.r.] – 7	I-III: 3 x 2 (30-sec)	I: n.r. II: n.r. III: n.r.	VAS n.r.-n.r. [n.r.]	Immediately [n.r.] 1 d [n.r.] 7 d [n.r.]
I and III: 3 x 11 [1] II and IV: 3 x 15 [1] V: 2h/daily (10)	3 x 3 min (1-min)	I and III: 470 and 810 / 350 and 200 / n.r. and n.r.	VAS 0-10 [Intensity of TS]	Immediately [0] 1 d [0] 2 d [0] 7 d [4]
I and III: 3 x 7,5 [1] II and IV: 3 x 15 [1]	I and III: 3 x 2 (30-sec)	I and III: 470 and 810 / 350 and 200 / n.r. and n.r.	VAS 0-10 [Intensity of TS]	Immediately [0] 1 d [0] 7 d [0]
I-II: 3 x 15 min [1]	I: 3 x 15 min (0-min)	I: 350-600 / n.r. / 0.2	VAS 0-10 [Intensity of TS]	Immediately [n.r.] 1 d [n.r.] 7 d [n.r.]

Table 2: *Summary of the Primary Studies Included in this Systematic Review (Continued)*

Study ID	Study Design [setting]	Subjects' Age, Mean ± SD [range] (y)	Number of Subjects [%] (male)	Baseline Color/ Evaluated Tooth	Groups and Materials/Number of Patients per Group
Papathanasiou, 2002[52]	Split-mouth [University]	n.r. ± n.r. [n.r.-n.r.]	n.r. [n.r.]	A_3/Anterior teeth	I: IO 35% HP^{d} + $light^{HL}$/20 II: IO 35% HP^{dLF}/20
Polydorou, 2013[14]†	Parallel [n.r.]	27.6 ± 5.00 [18-70]	n.r. [n.r.]	C_1/Upper Canines	I: IO 38% HP^{dLF}/20 II: IO 38% HP^{d} + $light^{HL}$/20 III: IO 38% HP^{d} + $light^{LA}$/20
Santos 2018[41]	Parallel [University]	n.r. ± n.r. [18-40]	n.r. [n.r.]	n.r./n.r.	I: $Light^{VL}$/20 II: IO 35% CP^{g} + $light^{VL}$/20 III: IO 35% HP^{bLF}/20 IV: $Light^{VL}$ + gingivoplasty/20
Strobl, 2010[53]	Split-mouth [n.r.]	n.r. ± n.r. [n.r-n.r.]	7 [35.0]	A_1/n.r.	I: IO 35% HP^{p} + $light^{LA}$/20 II: IO 35% HP^{pLF}/20
Tavares, 2003[39]	Parallel [n.r.]	44.0 ± n.r. [17-64]	38 [43.7]	D_4/Upper Incisors	I: IO 15% $HP^{n.r.}$ + $light^{PAC}$/29 II: IO 15% $HP^{n.r.LF}$/29 III: IO Placebo gel + $light^{PAC}$/29
Ward, 2012[54]	Split-mouth [n.r.]	37.0 ± n.r. [18-78]	12 [80]	A_3/Anterior teeth	I: 15% HP^{m} + $light^{MHL}$/15 II: 25% HP^{m} + $light^{MHL}$/15
Ziemba, 2005[40]	Parallel [Clinical]	n.r. ± n.r. [18-70]	[n.r.]	A_3/Anterior teeth	I: IO 25% HP^{k} + $light^{MHL}$/25 II IO 25% HP^{kLF}/25

Abbreviations: ID–identification; SD–standard deviation; y–year n.r.–not reported in the study; AH–At-Home bleaching; CP–Carbamide Peroxide; IO–In-Office bleaching; HP–Hydrogen Peroxide; VAS–Visual Analog Scale; TS–Tooth Sensitivity; NRS: Numeric Rating Scale; LF-light-free; HL-Halogen Lamp; LL-LED/Laser; LED-light-emitting diodes; MHL-Metal halide light; VL-Violet light; LA-Laser; PAC-Plasma arc lamp.

†The study entered in the meta-analysis twice, once in each subgroup.

[a] *Whiteness Perfect (FGM, Joinville, Santa Catarina, Brazil).*

[b] *Whiteness HP Maxx (FGM, Joinville, Santa Catarina, Brazil).*

[c] *Lase Peroxide Sensy (DMC, São Carlos, São Paulo, Brazil).*

[d] *Opalescence Xtra Boost (Ultradent Inc., South Jordan, Utah, United States).*

[e] *Lase Peroxide Lite (DMC, São Carlos, São Paulo, Brazil).*

[f] *Total Blanc (Nova DFL, Rio de Janeiro, Rio de Janeiro, Brazil).*

Table 2: *Summary of the Primary Studies Included in this Systematic Review (Extended)*

Bleaching Protocol	**Light Source**			
Applications x min [sessions] – interval (days)	**Light Protocol: Applications x time (interval)**	**Spectrum (nm) / Intensity, (mW/cm²) / Power output (W)**	**Tooth Sensitivity Scale [outcome]**	**Follow-up [Drop-outs]**
I-II: 1 x 20 min [1]	I: 1 x 20 min (0-min)	I: n.r. / n.r. / n.r.	Questionnaire [Risk of TS]	1 d [0]
I-III: 4 x 15 min [1]	II: 4 x 8 min (7-min) III: 4 x 30 sec (14,5-min)	II: 480-520 / n.r. / 150 III: 980 / n.r. / 6	Questionnaire [Risk of TS]	Immediatelly [0]
II-IV: 3 x 10 [4] – 7	I-II and IV: 20 x 1 min (30-sec)	I and II and IV: 390-410 / 112 / 1.2	VAS 0-100 [Risk of TS]	Immediatelly [n.r.] 7 d [n.r.] 14 d [n.r.] 21 d[n.r.] 30 d [n.r] 42 d [n.r.] 180 d [n.r.]
I-II: 2 x 1 min and 45 sec [2] – 7	I: 3 x 10 sec (n.r.)	I: 1064 µm / 1.4 J/cm² / 4	Questionnaire [Risk of TS]	Immediately [0]
I-III: 3 x 20 min [1]	I and III: 3 x 20 min (0-min)	I and III: 400-505 / 130-160 / n.r.	NRS 0-3 [Risk of TS]	Immediately [0] 7 d [0] 60 d [0] 180 d [0]
I-II: 3 x 20 min [1]	I-II: 3 x 20 min (0-min)	I-II: 400-505 / n.r. / n.r.	VAS 0-10 [Intensity of TS]	Immediately [0] 1 d [0] 7 d [0]
I-II: 3 x 15 min [1]	I: 3 x 15 min (0-min)	I: 365-500 / n.r. / n.r.	VAS 0-10 [Intensity of TS]	Immediately [0] 7 d [0] 30 d [1]

[g] Whiteform (Fórmula e Ação, São Paulo, São Paulo, Brazil).
[h] LaserWhite 10 (Biolase Technology Inc., San Clemente, California, United States).
[i] Remewhite (Remedent, Deurle, Belgium).
[j] By White (Biowhite, Ensodent, Italy).
[k] Zoom 2 (Discus Dental, Inc., Culver City, California, United States).
[l] BriteSmile (BriteSmile, Walnut Creek, California, United States).
[m] ZOOM Chairside Whitening System (Discus Dental, Inc., Culver City, Calilfornia, United States).
[n] White Gold Office (Dentsply, 38West Clarke Ave., Milford, United States).
[o] Opalescence PF (Ultradent, South Jordan, Utah, United States).
[p] Fotona (Fotona d.d., Ljubljana, Slovenia).

Age and Gender of The Patients in the Primary RCTs—

The patients ranged from 18 to 78 years old; ten studies did not report participant age.[31,37,43,46,47,49-53] The mean age of all participants included in the RCTs that reported this information was approximately 27.9 years, showing a predominance of young adults (Table 2). Females were predominant in most studies that reported this characteristic.[c]

Bleaching Protocols—

High-concentration HP. Twenty-four studies used high-concentration HP.[d] The concentration of the products employed were: 35%, 37%, 38% (varying from 35% to 38%) (Table 2).

Low-concentration HP. Seventeen studies used low-concentration HP.[e] The concentrations of the products employed were: 6%, 15%, 20%, 25% (varying from 6% to 25%); when 35% CP was used, the study was included in the low-concentration HP subgroup as 35% CP corresponds to approximately 12% active HP[58] (Table 2).

The application protocol of the in-office bleaching was quite varied. Several studies applied the product in three 15-minute applications in each clinical session.[f] However, variations with one to five applications per clinical session were also observed.

Most studies involved only a single clinical session,[g] but two to four clinical sessions with intervals between seven and 15 days were also observed (Table 2).

Different types of light activation were used. Six studies used halogen lamps,[14,24,33,45,52,57] eighteen used LEDs/lasers,[h] five used only LEDs,[24,30,33,42,45] seven used metal-halide light,[24,32,40,46,47,51,54] three used a violet light,[28,37,41] three used only a laser source,[14,30,53] and two used PACs[30,39] with various protocols.

Assessment of the RoB

The RoB of the eligible studies is presented in Figure 2. Six studies were classified as having low RoB,[27,36,39,44,48,50] and three were considered to have high RoB.[32,34,35,38] A few full-text studies reported the method of randomization and allocation concealment and therefore were classified as having unclear RoB.

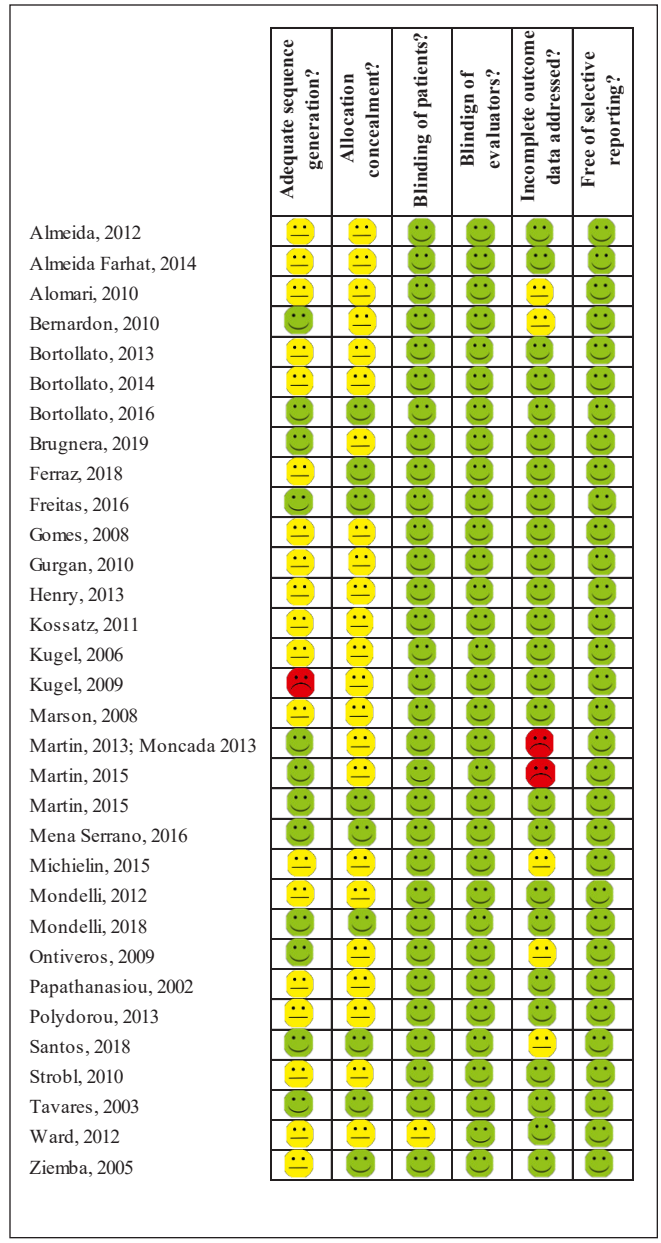

Figure 2. *Summary of the risk of bias assessment, according to the Cochrane Collaboration tool.*

Traditional and Network Meta-analysis

In this phase, thirteen eligible studies could not be meta-analyzed. The studies by Bortolatto (2014),[26] Bortolatto (2016),[27] Kugel (2006),[47] Martin (2015),[48] and Martin (2015)[35] were removed because the authors compared a low-concentration HP with a high-concentration HP. The studies by Henry (2013),[46] Michielin (2015),[37] Mondelli (2012),[49] Papathanasiou (2002),[52] Santos (2018),[41] and Strobl (2010)[53] were removed because the data could not be extracted. The studies by Ferraz (2018)[29] and Ward (2012)[54] were

[c] Ref. 24,28-30,34,36,38,39,46,53,56.
[d] Ref. 14,24-27,30,31,33-38,41-45,47-50,52,53,57.
[e] Ref. 26-29,32,34-41,46-48,51,54.
[f] Ref. 25,26,31,33-38,40,43-46,49-51.
[g] Ref. 14,24,30,32,34,35,38-40,46,47,49,50,52,54-56.
[h] Ref. 25-27,29,31,33-38,42-45,48-50,57.

removed because the authors did not have a common comparator group. In summary, nineteen studies were included in the meta-analysis. Thirteen studies had only two arms,[i] two studies had three arms,[14,57] and four studies had four arms.[24,30,33,45] The geometry of the evidence is presented in Figure 3. In the network figures, each node represents a treatment, and the line thickness represents the number of studies included in the comparison.

Risk of Tooth Sensitivity

Regarding the risk of TS, a total of five treatments with high-concentration products were compared in the network (Figure 3A), totaling ten pairs of comparisons with 351 patients. Direct evidence was available for eight pairs (Figure S1A) and no significant differences in risk among treatments were found. The results from the network meta-analysis are described in Figure 4 (lower diagonal). This network of evidence has some pairwise comparisons with only indirect evidence (LED vs. laser, for example) and six comparisons with both direct and indirect evidence, for which no inconsistency was found (Figure 5). Network results also show no difference among the five treatments.

In the consideration of products with low concentration, five treatments were compared (Figure 3B), totaling ten pairs of comparisons with 168 patients. Direct evidence was available for four pairs

[i] Ref. 25,28,31,32,34,36,38-40,42-44,50,51.

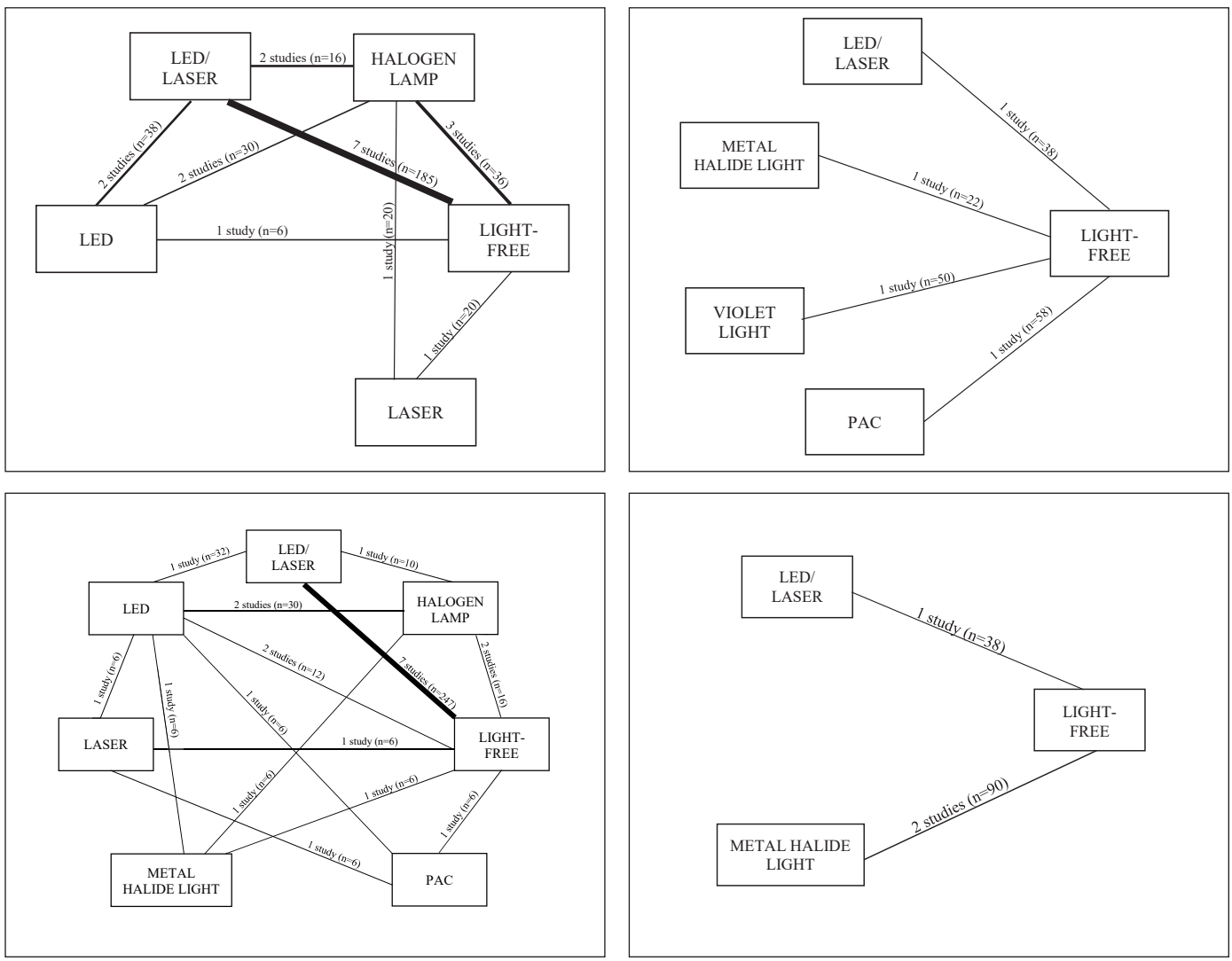

Figure 3. *Network of eligible comparisons. Risk of tooth sensitivity (TS) for: (A): High-concentration hydrogen peroxide (HP) and (B): Low-concentration HP. Intensity of TS for (C): High-concentration HP and (D): low-concentration HP.*
n = number of patients in the pair comparison.

PAC	--	0.47 (0.01, 13.6) VERY LOW[1,2,3]	0.77 (0.23, 2.40) VERY LOW[1,2,3]	--	1.10 (0.36, 3.20) VERY LOW[1,2,3]	--	1.20 (0.54, 2.60) LOW[1,2]
--	**Laser**	--	--	--	--	--	--
--	--	**Violet light**	1.60 (0.04, 11.0) VERY LOW[1,2,3]	--	2.20 (0.06, 14.9) VERY LOW[1,2,3]	--	2.50 (0.11, 10.6) LOW[1,2]
--	--	--	**Metal halide light**	--	1.40 (0.49, 4.40) VERY LOW[1,2,3]	--	1.60 (0.72, 3.80) LOW[1,2]
--	9.56 (0.98, 328.59) VERY LOW[1,2,3]	--	--	**LED**	--	--	--
--	9.98 (1.08, 339.94) VERY LOW[1,2,3]	--	--	1.10 (0.61, 1.90) LOW[1,2]	**LED/Laser**	--	1.10 (0.55, 2.40) LOW[1,2]
--	10.93 (1.23, 372.21) LOW[1,2]	--	--	1.10 (0.58, 2.20) LOW[1,2]	1.10 (0.56, 1.90) LOW[1,2]	**Halogen lamp**	--
--	9.48 (1.03, 323.79) LOW[1,2]	--	--	1.00 (0.50, 1.70) LOW[1,2]	0.96 (0.59, 1.30) MODERATE[1]	0.88 (0.44, 1.50) MODERATE[1]	**Light-free**

On the upper diagonal, the results are for the low-concentrate HP and RR are between the row-defining treatment and the column-defining treatment, RR<1 favors the row-defining treatment. The results on the lower diagonal are for high-concentrate HP and RR are between the column-defining treatment and the row-defining treatment, RR<1 favors the column-defining treatment. The 95% CrI that crosses the null value of 1 indicates that we do not have evidence to state significant difference between the two treatments compared.
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect
Explanations: 1. Risk of bias: most eligible studies are at unclear risk of bias; 2. Imprecision: Wide confidence interval that includes the null effect; 3. Indirectness: Information provided only by indirect evidence

Figure 4. *Mixed treatment comparison (MTC) results (risk ratio [RR] with 95% credible intervals [CrI]) and quality of evidence (gradings of recommendations assessment [GRADE]) for risk of tooth sensitivity (TS).*

(Figure S1B) and no significant differences in risk were found. As we can see from the geometry of the network (Figure 3B), the four pairs of comparisons have only direct evidence, with the light-free condition as the common comparator. The results from this network meta-analysis are described in Figure 4 (upper diagonal), which also shows that there was no evidence of difference among the five treatments.

Intensity of Tooth Sensitivity

Regarding the intensity of TS, a total of seven treatments with high concentration products were compared in the network (Figure 3C), totaling 21 pairs of comparisons with 395 patients. Direct evidence was available for 14 pairs (Figure S2A), and no significant differences in intensity were found. The results from the network meta-analysis are described in Figure 6 (lower diagonal). This network of evidence has some pairwise comparisons with only indirect evidence (PAC vs. metal halide light, for example) and six comparisons with both, direct and indirect evidence, for which no statistical inconsistency was found (Figure 7). When all treatments were analyzed together, no evidence of difference was found.

Considering products with low concentration, three treatments were compared (Figure 3D), totaling three pairs of comparisons with 128 patients. Direct evidence was available for two pairs (Figure S2B), and no significant differences in intensity were found. As we can see from the geometry of the network (Figure 3D), the pair comparing metal halide light to LED/laser has only direct evidence, with the light-free condition as the common comparator. The results from this

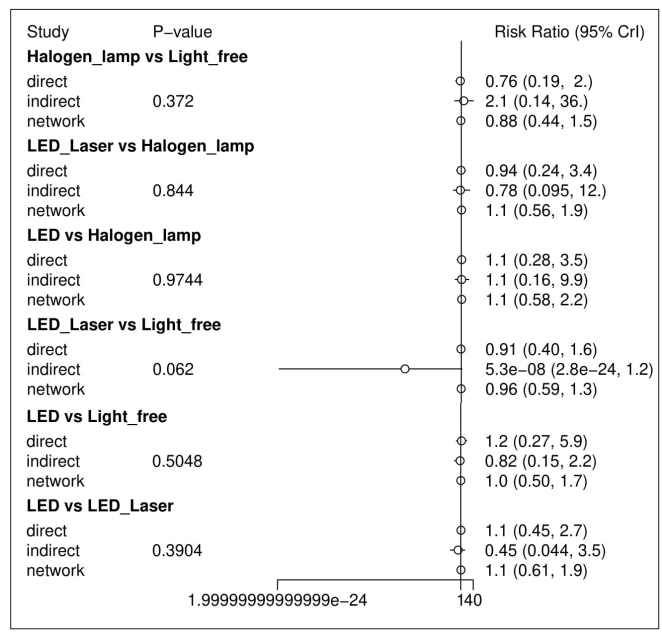

Figure 5. *Forest plot of the evaluation of the inconsistency assumption between direct and indirect evidence used in the network meta-analysis of the risk of tooth sensitivity (TS) for bleaching with high-concentrate hydrogen peroxide (HP) with different light activation methods (p<0.05 indicates inconsistency of the pairs).*

PAC	--	--	--	--	--	--	--
2.00 (-2.15, 6.14) LOW[1,2]	**Laser**	--	--	--	--	--	--
--	--	**Violet light**	--	--	--	--	--
0.24 (-4.67, 5.29) VERY LOW[1,2,3]	-1.75 (-6.79, 3.22) VERY LOW[1,2,3]	--	**Metal halide light**	--	0.35 (−2.60, 3.10) VERY LOW[1,2,3]	--	0.62 (−0.64, 2.10) LOW[1,2]
0.72 (-2.97, 4.50) LOW[1,2]	-1.27 (-5.05, 2.48) LOW[1,2]	--	-0.47 (-4.14, 3.10) LOW[1,2]	**LED**	--	--	--
0.67 (-3.24, 4.61) VERY LOW[1,2,3]	-1.34 (-5.23, 2.67) VERY LOW[1,2,3]	--	-0.41 (-4.20, 3.34) VERY LOW[1,2,3]	-0.05 (-2.40, 2.30) LOW[1,2]	**LED/Laser**	--	0.98 (−1.40, 3.50) LOW[1,2]
0.24 (-3.91, 4.46) VERY LOW[1,2,3]	-1.76 (-5.92, 2.46) VERY LOW[1,2,3]	--	0.01 (-3.66, 3.64) LOW[1,2]	0.49 (-2.00, 3.00) LOW[1,2]	0.44 (-2.10, 3.00) LOW[1,2]	**Halogen lamp**	--
0.05 (-3.7, 3.77) LOW[1,2]	-1.95 (-5.7, 1.83) LOW[1,2]	--	0.21 (-3.38, 3.80) LOW[1,2]	0.68 (-1.60, 2.90) LOW[1,2]	-0.62 (-2.10, 0.84) MODERATE[1]	0.19 (-2.20, 2.60) LOW[1,2]	**Light-free**

On the upper diagonal, the results are for the low-concentrate HP and MD are between the row-defining treatment and the column-defining treatment, MD positive favors the column-defining treatment. The results on the lower diagonal are for high-concentrate HP and SMD are between the column-defining treatment and the row-defining treatment, SMD positive favors the row-defining treatment. The 95% CrI that crosses the null value of 0 indicates that we do not have evidence to state significant difference between the two treatments compared.
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect
Explanations: 1. Risk of bias: most eligible studies are at unclear risk of bias; 2. Imprecision: Wide confidence interval that includes the null effect; 3. Indirectness: Information provided only by indirect evidence

Figure 6. *Mixed treatment comparison (MTC) results (mean difference [MD] with 95% credible intervals [CrI]) and quality of evidence (gradings of recommendations assessment [GRADE]) for intensity of tooth sensitivity (TS).*

network meta-analysis are described in Figure 6 (upper diagonal), which also shows no evidence of difference among the three treatments.

Sensitivity Analysis

In two studies that did not report the standard deviation (SD),[43,45,50] we imputed an SD based on the average of the coefficients of variation of the other studies that reported the same finding.[59] More extreme imputations (such as a value corresponding to the lowest coefficient of variation of the primary studies and a value that was as high as the reported mean) were evaluated in a sensitivity analysis, and no differences in the results reported here could be detected.

The studies by Almeida Farhat (2014),[42] Alomari (2010),[24] and Gomes (2008)[45] used NRS pain scale to measure the intensity of TS, so SMD was used to summarize the effect of high-concentration products on intensity of TS. We also performed a sensitivity analysis by removing these three studies and using MD. The same conclusions in MTC analysis were observed whether the MTC was run with MD or SMD effect measures.

Assessment of the Certainty of the Evidence

In general, the quality of evidence was graded as low, due to unclear RoB and imprecision (Figures 4 and 6). Some comparisons were graded as very low, due to an unclear RoB in the vast majority of the studies, as well as imprecision and indirectness.

DISCUSSION

Although network meta-analyses are very common in health areas such as medicine and pharmacy,[60-64] there are only a few available studies in the dental field.[17,65,66]

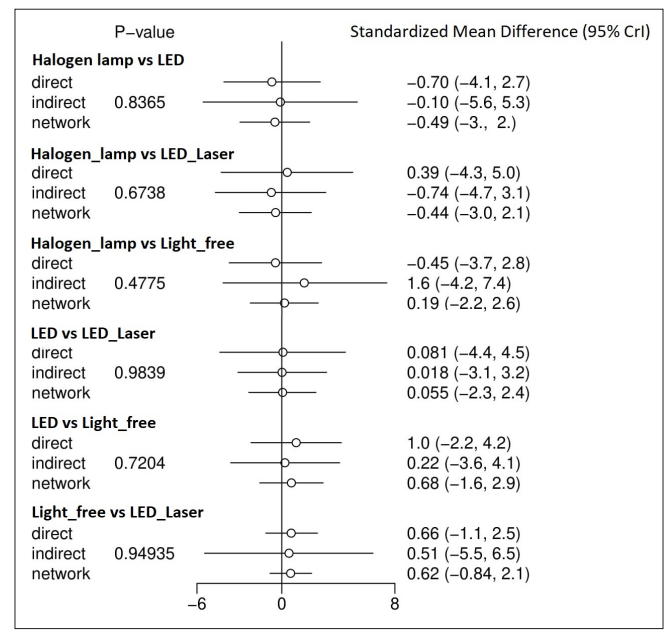

Figure 7. *Forest plot of the evaluation of the inconsistency assumption between direct and indirect evidence used in the network meta-analysis of the intensity of tooth sensitivity (TS) for bleaching with high-concentrate hydrogen peroxide (HP) with different light activation methods (p<0.05 indicates inconsistency of the pairs).*

Perhaps this low number of network meta-analyses reflects the small number of potential treatment options compared to the innumerable drugs available in medicine and pharmacy. Nevertheless, it is a valid method for making comparisons between treatments, because it allows for the aggregation of a larger amount of evidence, either direct or indirect, which comes from large or small clinical trials.[67-69] It allows the researcher to determine, among all available treatment options, which is the best[18] in terms of efficacy and safety.

This systematic review and network meta-analysis was conducted to evaluate the risk and intensity of TS for different types of light activation used for bleaching. TS is the most common adverse effect reported by patients during bleaching[70] and sometimes leads to treatment discontinuation.[32,71] Many studies have evaluated clinical alternatives to minimize this undesirable side effect. Administration of different types of medications (non-steroidal analgesics, anti-inflammatories, corticoids, opioids), application of topical desensitizers (based on potassium nitrate or fluoride), reduction of product concentration, and use of different bleaching protocols[23,50,71-74] have already been investigated.

Although in Europe the Scientific Committee on Cosmetic Products and Non-Food Products[75] recommends that tooth-bleaching products should contain between 0.1% and 6.0% hydrogen peroxide, this is not a rule worldwide. Such low-concentration products can be used in-office, but they are most commonly used in at-home protocols in countries where in-office bleaching with high-concentration HP is allowed.

While some researchers focus on the investigation of alternatives to reduce bleaching-induced TS, others focus on the investigation of protocols to improve bleaching efficacy, light activation being among the possible alternatives studied so far. It is widespread knowledge that light, *per se*, can catalyze the decomposition of HP into free radicals, the reason this product is usually sold in dark vials. However, the increased number of free radicals is not associated with improved bleaching efficacy, as stated in previous systematic reviews of the literature,[76-78] including one network meta-analysis.[17]

In addition to efficacy, the safety of alternative bleaching protocols requires investigation. It is desirable to know whether a bleaching protocol performed with any type of light can cause additional harm to the pulp. Theoretically, the higher quantity of free radicals produced by light activation could easily reach the pulp chamber and cause pulp inflammation[79,80] and chemical irritation, which may trigger pain transmission through sensory nerves.[25] Another issue that must be addressed in this discussion is that some light sources are no longer used in dentistry, such as PAC and halogen lamps. They were included in the present systematic review, however, as some clinicians may still have them in their offices. Additionally, they are important to provide improved network connectivity. Some *in vitro* studies have reported other disadvantages in using these light sources, such as the increase in pulp temperature, which is an additional source of damage to pulp tissue and TS.[81,82]

Few comparisons performed in this network meta-analysis found evidence that any type of light source was more harmful than others in terms of risk and intensity of TS, either for low- or high-concentration HP products. Network meta-analysis involves the pooling of individual study results, but the total number of trials in a network, the number of trials with more than two comparison arms, and heterogeneity may influence effect estimates.[83] For more significant evidence, the nodes of a network must be well connected, because the lack of specific comparisons creates uncertainty in the results.[84] This RCT highlights that there are many comparisons that lack either direct or indirect evidence, and this may serve as a research question for authors of RCTs.

Although all previous systematic reviews on this topic[17,76-78] have reported that light activation does not add any benefit to the whitening outcome, they have differed in their conclusions about high-concentration HP products. He and others (2012)[76] showed that light activation increases the intensity and the risk of TS during in-office bleaching, but this finding may be simply due to random bias, as few studies were eligible to be included by the time the study was conducted. Maran and others (2018)[77] only observed higher levels of TS when light activation was associated with low-concentration HP. In this study, Maran and others (2018)[85] compared light-activation bleaching to bleaching without light activation, thus increasing the power of the comparison and allowing the identification of a difference in the subgroup of low-concentration HP. SoutoMaior and others (2018)[78] observed lower levels of TS when light activation was used, but their meta-analysis presented some methodological flaws that made their conclusions unreliable; examples include inclusion of studies with more than one effect size without accounting for the fact that the same control group was employed in both estimates, and the choice of a fixed-effect rather than random-effects model.

In the present study, different light sources were evaluated individually, while in the previous systematic

review, data from different light sources were merged, increasing statistical power. However statistically significant results do not necessarily mean important clinical significance. Any small, clinically insignificant difference in effect size may be statistically significant if the sample size is large enough. Thus, care should be taken in evaluating statistically significant findings, and focus should be placed on the effect size and its precision.

The results of the present systematic review suggest that TS is neither exacerbated nor minimized by light activation with any type of light source. The amount of free radicals that reach the pulp with high- and low-concentration in-office bleaching products is already enough to reach the pulp chamber, causing cellular damage[86] and TS.[77] Because the quality of evidence was graded as low or very low for most of the comparisons, our confidence in the effect estimates generated is limited, because the true effect may be substantially different from what is reported here.

The reasons for downgrading the certainty of evidence are related to the unclear RoB of eligible studies and imprecision. Lack of description of how the random sequence was generated and how allocation concealment was guaranteed were the main reasons studies were considered to have an unclear RoB. The report of RCTs in accordance with the CONSORT statement[87] is deficient in bleaching studies,[j] preventing review authors from evaluating the method of random sequence and allocation concealment. This deficiency highlights the need to conduct more rigorous studies to answer this specific research question. By using appropriate methods of randomization, allocation concealment, and examiner blinding, RCTs with low RoB may be published, producing more reliable conclusions.

Another critical topic to be evaluated in meta-analysis is the size of the statistical heterogeneity. Differences in methods, study design, study populations, the composition of materials, definitions, and measurements of outcome, follow-up, or other features make trials different,[84] and therefore trials usually estimate effect sizes specific to the population they represent. If the heterogeneity is substantial, the point estimate produced by the meta-analysis may not serve as a good estimator of the effect size in different populations. Unfortunately, due to the low number of studies included in this network meta-analysis, heterogeneity in each pairwise comparison was difficult to assess, because the low number of studies produced imprecise estimates of heterogeneity.

[j] Ref. 13,14,23-26,30,31,37,42,45-47,49,52-54.

CONCLUSIONS

We did not find evidence that the use of any type of light source causes increased risk and intensity of TS. However, for the majority of comparisons, the quality of evidence was graded as low or very low, limiting our confidence in the conclusions.

Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

Supplemental Data

Figures S1 and S2 are available online at https://meridian.allenpress.com/operative-dentistry.

(Accepted 21 December 2020)

REFERENCES

1. Silva FBD, Chisini LA, Demarco FF, Horta BL, & Correa MB (2018) Desire for tooth bleaching and treatment performed in Brazilian adults: Findings from a birth cohort *Brazilian Oral Research* **32** e12. http://dx.doi.org/10.1590/1807-3107bor-2018.vol32.0012

2. Afshar MK, Eskandarizadeh A, Torabi M, Mousavi MJ, & Mohammadzadeh I (2019) Patient satisfaction with dental appearance and related factors—A cross sectional study *Journal of Evolution of Medical and Dental Sciences* **8(48)** 3569-3575. http://dx.doi.org/10.14260/jemds/2019/77

3. Tin-Oo MM, Saddki N, & Hassan N (2011) Factors influencing patient satisfaction with dental appearance and treatments they desire to improve aesthetics *BMC Oral Health* **11** 6. https://doi.org/10.1186/1472-6831-11-6

4. Fernández E, Bersezio C, Bottner J, Avalos F, Godoy I, Inda D, Vildosola P, Saad J, Oliveira Jr O, & Martin J (2016) Longevity, esthetic perception, and psychosocial impact of teeth bleaching by low (6%) hydrogen peroxide concentration for in-office treatment: A randomized clinical trial *Operative Dentistry* **42(1)** 41-52. http://dx.doi.org/10.2341/15-335-C

5. Dahl J & Pallesen U (2003) Tooth bleaching—A critical review of the biological aspects *Critical Reviews in Oral Biology and Medicine* **14(4)** 292-304. http://dx.doi.org/10.1177/154411130301400406

6. Cardenas AFM, Maran BM, Araújo LCR, De Siqueira FSF, Wambier LM, Gonzaga CC, Loguercio AD, & Reis A (2019) Are combined bleaching techniques better than their sole application? A systematic review and meta-analysis *Clinical Oral Investigations* 1-17. http://dx.doi.org/10.1007/s00784-019-03042-4

7. Eimar H, Siciliano R, Abdallah M-N, Nader SA, Amin WM, Martinez P-P, Celemin A, Cerruti M, & Tamimi F (2012) Hydrogen peroxide whitens teeth by oxidizing the organic structure *Journal of Dentistry* **40** e25-e33. http://dx.doi.org/10.1016/j.jdent.2012.08.008

8. Costa JB, Mcpharlin R, Paravina RD, & Ferracane JL (2010) Comparison of at-home and in-office tooth whitening using a novel shade guide *Operative Dentistry* **35(4)** 381-8. http://dx. doi: 10.2341/09-344-C

9. De Silva Gottardi M, Brackett MG, & Haywood VB (2006) Number of in-office light-activated bleaching treatments needed to achieve patient satisfaction *Quintessence International* **37(2)** 115-120.

10. Basting RT, Amaral FL, Franca FM, & Florio FM (2012) Clinical comparative study of the effectiveness of and tooth sensitivity to 10% and 20% carbamide peroxide home-use and 35% and 38% hydrogen peroxide in-office bleaching materials containing desensitizing agents *Operative Dentistry* **37(5)** 464-473. http://dx.doi.org/10.2341/11-337-c

11. Mena-Serrano AP, Parreiras S, Nascimento ED, Borges C, Berger S, Loguercio A, & Reis A (2015) Effects of the concentration and composition of in-office bleaching gels on hydrogen peroxide penetration into the pulp chamber *Operative Dentistry* **40(2)** E76-E82. http://dx.doi.org/10.2341/13-352-L

12. Reis A, Tay L, Herrera D, Kossatz S, & Loguercio A (2011) Clinical effects of prolonged application time of an in-office bleaching gel *Operative Dentistry* **36(6)** 590-596. http://dx.doi.org/10.2341/10-173-C

13. Marson F, Sensi L, Strassler H, Miraziz L, Riehl H & Reis R (2008) In-office bleaching gel application times: clinical evaluation *Journel of Dental Resarch* **87(Special Issue B)** 1028. http://dx.doi.org/10.2341/07-57

14. Polydorou O, Wirsching M, Wokewitz M, & Hahn P (2013) Three-month evaluation of vital tooth bleaching using light units-a randomized clinical study *Operative Dentistry* **38(1)** 21-32. http://dx.doi.org/10.2341/12-041-C

15. Buchalla W & Attin T (2007) External bleaching therapy with activation by heat, light or laser - A systematic review *Dental Materials Journal* **23(5)** 586-596. http://dx.doi.org/10.1016/j.dental.2006.03.018

16. Dunn WJ & Bush AC (2002) A comparison of polymerization by light-emitting diode and halogen-based light-curing units *Journal of the American Dental Association* **133(3)** 335-341. http://dx.doi.org/10.14219/jada.archive.2002.0173

17. Maran BM, Ziegelmann PK, Burey A, De Paris Matos T, Loguercio AD, & Reis A (2019) Different light-activation systems associated with dental bleaching: A systematic review and a network meta-analysis *Clinical Oral Investigations* **23(4)** 1499-1512. http://dx.doi.org/10.1007/s00784-019-02835-x

18. Tonin FS, Rotta I, Mendes AM, & Pontarolo R (2017) Network meta-analysis: a technique to gather evidence from direct and indirect comparisons *Pharmacy Practice (Granada)* **15(1)** 943. http://dx.doi.org/10.18549/PharmPract.2017.01.943

19. Lu G & Ades A (2004) Combination of direct and indirect evidence in mixed treatment comparisons *Statistics in Medicine* **23(20)** 3105-3124. http://dx.doi.org/10.1002/sim.1875

20. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, Ioannidis JP, Straus S, Thorlund K, & Jansen JP (2015) The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: Checklist and explanations *Annals of Internal Medicine* **162(11)** 777-784. http://dx.doi.org/10.7326/M14-2385

21. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA, Cochrane Bias Methods Group & Cochrane Statistical Methods Group (2011) The Cochrane Collaboration's tool for assessing risk of bias in randomised trials *British Medical Journal* **343** d5928. http://dx.doi.org/10.1136/bmj.d5928

22. Dias S, Welton N, Caldwell D, & Ades A (2010) Checking consistency in mixed treatment comparison meta-analysis *Statistics in Medicine* **29(7-8)** 932-944. http://dx.doi.org/ 10.1002/sim.3767

23. Almeida LC, Costa CA, Riehl H, Dos Santos PH, Sundfeld RH, & Briso AL (2012) Occurrence of sensitivity during at-home and in-office tooth bleaching therapies with or without use of light sources *Acta Odontologica Latinoamericana* **25(1)** 3-8.

24. Alomari Q & El Daraa E (2010) A randomized clinical trial of in-office dental bleaching with or without light activation *Journal of Contemporary Dental Practice* **11(1)** e17-e24.

25. Bortolatto JF, Pretel H, Neto CS, Andrade MF, Moncada G, & Junior OBO (2013) Effects of LED–laser hybrid light on bleaching effectiveness and tooth sensitivity: A randomized clinical study *Laser Physics Letters* **10(8)** 085601. http://dx.doi.org/10.1088/1612-2011/10/8/085601

26. Bortolatto J, Pretel H, Floros M, Luizzi A, Dantas AAR, Fernandez E, Moncada G, & De Oliveira Jr O (2014) Low concentration H2O2/TiO_N in office bleaching: A randomized clinical trial *Journal of Dental Research* **93(7 supplement)** 66S-71S. http://dx.doi.org/10.1177/0022034514537466

27. Bortolatto JF, Trevisan TC, Bernardi PSI, Fernandez E, Dovigo LN, Loguercio AD, Batista De Oliveira Junior O, & Pretel H (2016) A novel approach for in-office tooth bleaching with 6 % H2O2/TiO_N and LED/laser system—A controlled, triple-blinded, randomized clinical trial *Lasers in Medical Science* **31(3)** 437-444. http://dx.doi.org/10.1007/s10103-016-1866-2

28. Brugnera AP, Nammour S, Rodrigues JA, Mayer-Santos E, De Freitas PM, Brugnera Junior A, & Zanin F (2020) Clinical evaluation of in-office dental bleaching using a violet LED *Photobiomodulation, Photomedicine, and Laser Surgery* **38(2)** 98-104. http://dx.doi.org/10.1089/photob.2018.4567

29. Ferraz NKL, Nogueira LC, Neiva IM, Ferreira RC, Moreira AN, & Magalhães CS (2019) Longevity, effectiveness, safety, and impact on quality of life of low-concentration hydrogen peroxides in-office bleaching: A randomized clinical trial *Clinical Oral Investigations* **23(5)** 2061-2070. http://dx.doi.org/10.1007/s00784-018-2607-7

30. Gurgan S, Cakir FY, & Yazici E (2010) Different light-activated in-office bleaching systems: A clinical evaluation *Lasers in Medical Science* **25(6)** 817-822. http://dx.doi.org/10.1007/s10103-009-0688-x

31. Kossatz S, Dalanhol AP, Cunha T, Loguercio A, & Reis A (2011) Effect of light activation on tooth sensitivity after in-office bleaching *Operative Dentistry* **36(3)** 251-257. http://dx.doi.org/10.2341/10-289-C

32. Kugel G, Ferreira S, Sharma S, Barker ML, & Gerlach RW (2009) Clinical trial assessing light enhancement of in-office tooth whitening: Masters of esthetic dentistry *Journal of Esthetic and Restorative Dentistry* **21(5)** 336-347. http://dx.doi.org/10.1111/j.1708-8240.2009.00287.x

33. Marson FC, Sensi LG, Vieira LCC, & Araujo E (2008) Clinical evaluation of in-office dental bleaching treatments with and without the use of light-activation sources *Operative Dentistry* **33(1)** 15-22. http://dx.doi.org/10.2341/07-57

34. Martin J, Fernandez E, Bahamondes V, Werner A, Elphick K, Oliveira Jr OB, & Moncada G (2013) Dentin hypersensitivity after teeth bleaching with in-office systems. Randomized clinical trial *American Journal of Dentistry* **26(1)** 10-14.

35. Martin J, Ovies N, Cisternas P, Fernández E, Junior OO, De Andrade M, Moncada G, & Vildósola P (2015) Can an LED-laser hybrid light help to decrease hydrogen peroxide concentration while maintaining effectiveness in teeth bleaching? *Laser Physics* **25(2)** 025608. http://dx.doi.org/10.1088/1054-660X/25/2/025608

36. Mena-Serrano A, Garcia E, Luque-Martinez I, Grande R, Loguercio A, & Reis A (2016) A single-blind randomized trial about the effect of hydrogen peroxide concentration on light-activated bleaching *Operative Dentistry* **41(5)** 455-464. http://dx.doi.org/10.2341/15-077-C

37. Michielin M, Trentino A, Bombonatti JFS, & Mondelli RF (2015) Randomized vital teeth bleaching with light source: 6 month follow-up *Journal of Dental Research* **94(Special Issue A)** 3668.

38. Moncada G, Sepúlveda D, Elphick K, Contente M, Estay J, Bahamondes V, Fernandez E, Oliveira O, & Martin J (2013) Effects of light activation, agent concentration, and tooth thickness on dental sensitivity after bleaching *Operative Dentistry* **38(5)** 467-476. http://dx.doi.org/10.2341/12-335-C

39. Tavares M, Stultz J, Newman M, Smith V, Kent R, Carpino E, & Goodson JM (2003) Light augments tooth whitening with peroxide *Journal of the American Dental Association* **134(2)** 167-175. http://dx.doi.org/10.14219/jada.archive.2003.0130

40. Ziemba SL, Felix H, Macdonald J, & Ward M (2005) Clinical evaluation of a novel dental whitening lamp and light-catalyzed peroxide gel *Journal of Clinical Dentistry* **16(4)** 123-127.

41. Dos Santos AECG, Bussadori SK, Pinto MM, Junior DaP, Brugnera Jr A, Zanin FaA, Rodrigues MFSD, Motta LJ, & Horliana ACRT (2018) Evaluation of in-office tooth whitening treatment with violet LED: Protocol for a randomised controlled clinical trial *British Medical Journal Open* **8(9)** e021414. http://dx.doi.org/10.1136/bmjopen-2017-021414

42. De Almeida Farhat PB, Santos FA, Gomes JC, & Gomes OM (2014) Evaluation of the efficacy of LED-laser treatment and control of tooth sensitivity during in-office bleaching procedures *Photomedicine Laser Surgery* **32(7)** 422-426. http://dx.doi.org/10.1089/pho.2014.3729

43. Bernardon JK, Sartori N, Ballarin A, Perdigao J, Lopes G, & Baratieri LN (2010) Clinical performance of vital bleaching techniques *Operative Dentistry* **35(1)** 3-10. http://dx.doi.org/10.2341/09-008cr

44. De Freitas PM, Menezes AN, Da Mota AC, Simoes A, Mendes FM, Lago AD, Ferreira LS, & Ramos-Oliveira TM (2016) Does the hybrid light source (LED/laser) influence temperature variation on the enamel surface during 35% hydrogen peroxide bleaching? A randomized clinical trial *Quintessence International* **47(1)** 61-73. http://dx.doi.org/10.3290/j.qi.a34454

45. Gomes RS, Souza FBD, Lacerda CM, Brambilla CFF, & Pascotto RC (2008) Avaliação clínica da eficiência do uso do sistema LED-laser, LED e luz halógena na ativação do agente clareador em dentes vitalizados *Revista. dental press de estética* **5(2)** 62-77.

46. Henry RK, Bauchmoyer SM, Moore W, & Rashid RG (2013) The effect of light on tooth whitening: A split-mouth design *International Journal of Dental Hygiene* **11(2)** 151-154. http://dx.doi.org/10.1111/j.1601-5037.2012.00568.x

47. Kugel G, Papathanasiou A, Williams AJ, Anderson C, & Ferreira S (2006) Clinical evaluation of chemical and light-activated tooth whitening systems *Compendium of Continuing Education in Dentistry Supplement* **27(1)** 54-62.

48. Martín J, Vildosola P, Bersezio C, Herrera A, Bortolatto J, Saad JR, Oliveira OB, Jr, & Fernandez E (2015) Effectiveness of 6% hydrogen peroxide concentration for tooth bleaching—A double-blind, randomized clinical trial *Journal of Dentistry* **43(8)** 965-972. http://dx.doi.org/10.1016/j.jdent.2015.05.011

49. Mondelli RFL, De Azevedo JFDG, Francisconi AC, De Almeida CM, & Ishikiriama SK (2012) Comparative clinical study of the effectiveness of different dental bleaching methods—Two year follow-up *Journal of Applied Oral Science* **20(4)** 435-443. http://dx.doi.org/10.1590/S1678-77572012000400008

50. Mondelli RFL, Rizzante FaP, Rosa ER, Borges AFS, Furuse AY, & Bombonatti JFS (2018) Effectiveness of LED/Laser irradiation on in-office dental bleaching after three years *Operative Dentistry* **43(1)** 31-37. http://dx.doi.org/10.2341/16-208-C

51. Ontiveros JC & Paravina RD (2009) Color change of vital teeth exposed to bleaching performed with and without supplementary light *Journal of Dentistry* **37(11)** 840-847. http://dx.doi.org/10.1016/j.jdent.2009.06.015

52. Papathanasiou A, Kastali S, Perry RD, & Kugel G (2002) Clinical evaluation of a 35% hydrogen peroxide in-office whitening system *Compendium of Continuing Education in Dentistry Supplement* **23(4)** 335-338.

53. Strobl A, Gutknecht N, Franzen R, Hilgers RD, Lampert F, & Meister J (2010) Laser-assisted in-office bleaching using a neodymium:yttrium-aluminum-garnet laser: an in vivo study *Lasers in Medical Science* **25(4)** 503-509. http://dx.doi.org/10.1007/s10103-009-0675-2

54. Ward M & Felix H (2012) A clinical evaluation comparing two H2O2 concentrations used with a light-assisted chairside tooth whitening system *Compendium of Continuing Education in Dentistry* **33(4)** 286-291.

55. Ontiveros JC (2011) In-office vital bleaching with adjunct light *Dental Clinics of North America* **55(2)** 241-253. http://dx.doi.org/10.1016/j.cden.2011.01.002

56. De Freitas PM, Menezes AN, Da Mota AC, Simoes A, Mendes FM, Lago AD, Ferreira LS, & Ramos-Oliveira TM (2016) Does the hybrid light source (LED/laser) influence temperature variation on the enamel surface during 35% hydrogen peroxide bleaching? A randomized clinical trial *Quintessence International* **47(1)** 61-73. http://dx.doi.org/10.3290/j.qi.a34454

57. Almeida LCA, Riehl H, Dos Santos PH, Sundfeld MLMM, & Briso ALF (2012) Clinical evaluation of the effectiveness of different bleaching therapies in vital teeth *International Journal of Periodontics and Restorative Dentistry* **32(3)** 302-309. http://dx.doi.org/10.1038/sj.bdj.2012.587

58. Da Costa JB, Mcpharlin R, Hilton T, Ferracane JL, & Wang M (2012) Comparison of two at-home whitening products of similar peroxide concentration and different delivery methods *Operative Dentistry* **37(4)** 333-339. http://dx.doi.org/10.2341/11-053-c

59. Ma J, Liu W, Hunter A, & Zhang W (2008) Performing meta-analysis with incomplete statistical information in clinical trials *BMC Medical Research Methodology* **8(1)** 56. http://dx.doi.org/10.1186/1471-2288-8-56

60. Bangalore S, Toklu B, Amoroso N, Fusaro M, Kumar S, Hannan EL, Faxon DP, & Feit F (2013) Bare metal stents, durable polymer drug eluting stents, and biodegradable polymer drug eluting stents for coronary artery disease: mixed treatment comparison meta-analysis *British Medical Journal* **347** f6625. http://dx.doi.org/10.1136/bmj.f6625

61. Rheinheimer J, Ziegelmann PK, Carlessi R, Reck LR, Bauer AC, Leitao CB, & Crispim D (2014) Different digestion enzymes used for human pancreatic islet isolation: a mixed treatment comparison (MTC) meta-analysis *Islets* **6(4)** e977118. http://dx.doi.org/10.4161/19382014.2014.977118

62. Ribeiro RA, Ziegelmann PK, Duncan BB, Stella SF, Da Costa Vieira JL, Restelatto LMF, Moriguchi EH, & Polanczyk CA (2013) Impact of statin dose on major cardiovascular events: A mixed treatment comparison meta-analysis involving more than 175,000 patients *International Journal of Cardiologyl* **166(2)** 431-439. http://dx.doi.org/10.1016/j.ijcard.2011.10.128

63. Sekine L, Morais VD, Lima KM, Onsten TG, Ziegelmann PK, & Ribeiro RA (2015) Conventional and high-dose daunorubicin and idarubicin in acute myeloid leukaemia remission induction treatment: A mixed treatment comparison meta-analysis of 7258 patients *Hematological Oncology* **33(4)** 212-219. http://dx.doi.org/10.1002/hon.2173

64. George JN, Woodson RD, Kiss JE, Kojouri K, & Vesely SK (2006) Rituximab therapy for thrombotic thrombocytopenic purpura: A proposed study of the Transfusion Medicine/Hemostasis Clinical Trials Network with a systematic review of rituximab therapy for immune- mediated disorders *Journal of Clinical Apheresis* **21(1)** 49-56. http://dx.doi.org/10.1002/jca.20091

65. Faggion Jr CM, Chambrone L, Listl S, & Tu YK (2013) Network meta- analysis for evaluating interventions in implant dentistry: the case of peri- implantitis treatment *Clinical Implant Dentistry and Related Research* **15(4)** 576-588. http://dx.doi.org/10.1111/j.1708-8208.2011.00384.x

66. Schwendicke F, Paris S, & Tu Y-K (2015) Effects of using different criteria for caries removal: A systematic review and network meta-analysis *Journal of Dentistry* **43(1)** 1-15. http://dx.doi.org/10.1016/j.jdent.2014.10.004

67. Walsh T, Worthington H, Glenny A, Appelbe P, Marinho V, & Shi X (2010) Fluoride toothpastes of different concentrations for preventing dental caries in children and adolescents *Cochrane Database of Systematic Reviews* **Jan 20(1)** CD007868. http://dx.doi.org/10.1002/14651858.CD007868.pub2

68. Jansen JP, Crawford B, Bergman G & Stam W (2008) Bayesian meta- analysis of multiple treatment comparisons: An introduction to mixed treatment comparisons *Value in Health* **11(5)** 956-964. http://dx.doi.org/10.1111/j.1524-4733.2008.00347.x

69. Caldwell DM, Dias S, & Welton NJ (2015) Extending treatment networks in health technology assessment: how far should we go? *Value in Health* **18(5)** 673-681. http://dx.doi.org/10.1016/j.jval.2015.03.1792

70. Kihn PW (2007) Vital tooth whitening *Dental Clinics of North America* **51(2)** 319-331. http://dx.doi.org/10.1016/j.cden.2006.12.001

71. De Paula EA, Kossatz S, Fernandes D, Loguercio AD, & Reis A (2014) Administration of ascorbic acid to prevent bleaching-induced tooth sensitivity: A randomized triple-blind clinical trial *Operative Dentistry* **39(2)** 128-135. http://dx.doi.org/10.2341/12-483-c

72. Charakorn P, Cabanilla L, Wagner W, Foong W, Shaheen J, Pregitzer R, & Schneider D (2009) The effect of preoperative ibuprofen on tooth sensitivity caused by in-office bleaching *Operative Dentistry* **34(2)** 131-135. http://dx.doi.org/10.2341/08-33

73. Maghaireh GA, Alzraikat H, & Guidoum A (2014) Assessment of the effect of casein phosphopeptide-amorphous calcium phosphate on postoperative sensitivity associated with in-office vital tooth whitening *Operative Dentistry* **39(3)** 239-247. http://dx.doi.org/10.2341/12-527-c

74. Klaric-Sever E, Budimir Z, Cerovac M, Stambuk M, Par M, Negovetic Vranic D, & Tarle Z (2018) Clinical and patient reported outcomes of bleaching effectiveness *Acta Odontologica Scandinavica* **76(1)** 30-38. http://dx.doi.org/10.1080/00016357.2017.1376111

75. Authority EFS (2007) Opinion of the Scientific Committee related to uncertainties in dietary exposure assessment *EFSA Journal* **5(1)** 438.

76. He LB, Shao MY, Tan K, Xu X, & Li JY (2012) The effects of light on bleaching and tooth sensitivity during in-office vital bleaching: A systematic review and meta-analysis *Journal of Dentistry* **40(8)** 644-653. http://dx.doi.org/10.1016/j.jdent.2012.04.010

77. Maran BM, Burey A, De Paris Matos T, Loguercio AD, & Reis A (2018) In-office dental bleaching with light vs. without light: A systematic review and meta-analysis *Journal of Dentistry* **70(1)** 1-13. http://dx.doi.org/10.1016/j.jdent.2017.11.007

78. SoutoMaior J, De Moraes S, Lemos C, Vasconcelos BDE, Montes M, & Pellizzer E (2018) Effectiveness of light sources on in-office dental bleaching: A systematic review and meta-analyses *Operative Dentistry* **44(3)** E105-E117. http://dx.doi.org/10.2341/17-280-L

79. Sulieman M, Rees J, & Addy M (2006) Surface and pulp chamber temperature rises during tooth bleaching using a diode laser: a study in vitro *British Dental Journal* **200(11)** 631-634. http://dx.doi.org/10.1038/sj.bdj.4813644

80. Eldeniz AU, Usumez A, Usumez S, & Ozturk N (2005) Pulpal temperature rise during light- activated bleaching *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **72(2)** 254-259. http://dx.doi.org/10.1002/jbm.b.30144

81. Bansal A, Kumar Y, Jindal N, Aggarwal R, & Jain S (2020) Evaluation of rise in pulp chamber temperature after activation with different curing lights on bleached teeth—An in vitro study *Dental Journal of Advance Studies 2020*, **8(03)**: 080-083. http://dx.doi.org/10.10 55/s-0040-1713693

82. Mondelli RFL, Soares AF, Pangrazio EGK, Wang L, Ishikiriama SK, & Bombonatti JFS (2016) Evaluation of temperature increase during in-office bleaching *Journal of Applied Oral Science* **24(2)** 136-141.

83. Hutton B, Salanti G, Chaimani A, Caldwell DM, Schmid C, Thorlund K, Mills E, Catala-Lopez F, Turner L, & Altman DG (2014) The quality of reporting methods and results in network meta-analyses: an overview of reviews and suggestions for improvement *PLoS One* **9(3)** e92508. http://dx.doi.org/10.7326/M14-2385

84. Mills EJ, Ghement I, O'regan C, & Thorlund K (2011) Estimating the power of indirect comparisons: a simulation study *PLoS One* **6(1)** e16237. http://dx.doi.org/10.1371/journal.pone.0016237

85. Maran BM (2018) In-office dental bleaching with light vs. without light: A systematic review and meta-analysis *British Dental Journal* **224** 622. http://dx.doi.org/10.1038/sj.bdj.2018.331

86. Torres CRG, Wiegand A, Sener B, & Attin T (2010) Influence of chemical activation of a 35% hydrogen peroxide bleaching gel on its penetration and efficacy-In vitro study *Journal of Dentistry* **38(10)** 838-846. http://dx.doi.org/10.1016/j.jdent.2010.07.002

87. Schulz KF, Altman DG, Moher D, & Group C (2011) CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials *International Journal of Surgery* **9(8)** 672-677. http://dx.doi.org/10.1136/bmj.c332

©Operative Dentistry, 2022, **47-2**, 236-237

Departments

Errata

Operative Dentistry apologizes for the errors in the following manuscripts.

AD Loguercio, LJC Vargas, MW Favoreto, HF Andrade, CP F Borges, A Dávila-Sánchez, A Reis, CP Mora; Effects of Microabrasion Prior to In-office Bleaching on Hydrogen Peroxide Permeability, Color Change, and Enamel Morphology. *Oper Dent* 1 November 2021 **46(6)** 661-668. doi: https://doi.org/10.2341/20-179-L

There are errors in the author order and contact list. The correct author order and author affiliations list should read (corrections are underlined):

LJ Calderón-Vargas • MW Favoreto • HF Andrade • CPF Borges • A Dávila-Sánchez • A Reis • C Pulido • AD Loguercio

Lina Johanna Calderón Vargas, DDS, Department of Oral Health, National University of Colombia, Bogotá, Colombia

Michael W Favoreto, DDS, MS student, Department of Restorative Dentistry, State University of Ponta Grossa, Parana, Brazil

Heloisa F Andrade, DDS, MS student, Department of Restorative Dentistry, State University of Ponta Grossa, Parana, Brazil

Christiane Philippini F Borges, DDs, MS, PhD, Department of Chemistry, State University of Ponta Grossa, Parana, Brazil

Andrés Dávila-Sánchez, DDS, MS, PhD, Universidad San Francisco de Quito USFQ, School of Dentistry, Department of Restorative Dentistry, Quito, Ecuador

Alessandra Reis, DDS, PhD, Department of Restorative Dentistry, State University of Ponta Grossa, Parana, Brazil

Camilo Pulido, DDS, MS, PhD, Universidad San Francisco de Quito USFQ, School of Dentistry, Department of Restorative Dentistry, Quito, Ecuador

*Alessandro D Loguercio, PhD, State University of Ponta Grossa, Ponta Grossa, Parana, Brazil

*Corresponding author: State University of Ponta Grossa, Dental Post-Graduate Program, Rua Carlos Cavalcanti, 4748, Bloco M - Uvaranas, Ponta Grossa, Paraná, Brazil; email: aloguercio@hotmail.com

Additionally, the legend in Table 3 should read:

*Identical uppercase or lowercase letters in each column indicate statistically similar means (one-way ANOVA and Tukey test, α=0.05).

D Kaisarly, M ElGezawi, R Haridy, A Elembaby, A Aldegheishem, R Alsheikh, KS Almulhim; Reliability of Class II Bulk-fill Composite Restorations With and Without Veneering: A Two-year Randomized Clinical Control Study. *Oper Dent* 1 September 2021 **46(5)** 491-504. doi: https://doi.org/10.2341/19-290-C

There are errors in the author order and contact list and corresponding author information. The correct author order, author affiliations list, and corresponding author information should read (corrections are underlined):

M ElGezawi • R Haridy • A Elembaby • A Aldegheishem • R Alsheikh • KS Almulhim • D Kaisarly

Moataz ElGezawi, BDS, MDSc, DDSc, Department of Restorative Dental Sciences, College of Dentistry, Imam Abdul Rahman Bin Faisal University, Dammam, Saudi Arabia

Rasha Haridy, BDS, MScD, PhD, Conservative Dentistry Department, College of Dentistry, Cairo University, Department of Clinical Dental Sciences, College of Dentistry, Princess Nourah bint Abdulrahman University, Saudi Arabia

Abeer Elembaby, BDS, MScD, PhD, Department of Restorative Dental Sciences, College of Dentistry, Imam Abdul Rahman Bin Faisal University, Dammam, Saudi Arabia

Alhanooof Aldegheishem, BDS, MScD, PhD, Department of Clinical Dental Sciences, Princess Nourah bint Abdulrahman University, Saudi Arabia

Rasha Alsheikh, BDS, MScD, PhD, Department of Restorative Dental Sciences, College of Dentistry, Imam Abdul Rahman Bin Faisal University, Dammam, Saudi Arabia

Khalid S. Almulhim BDS, MScD, PhD, Department of Restorative Dental Sciences, College of Dentistry,

Imam Abdul Rahman Bin Faisal University, Dammam, Saudi Arabia

*Dalia Kaisarly, BDS, MDSc, PhD, Department of Conservative Dentistry and Periodontology, University Hospital, LMU Munich, Munich, Germany

*Corresponding author: Poliklinik für Zahnerhaltung und Parodontologie Klinikum der Universität München Campus Innenstadt, Goethestraße 70, 80336 München, Germany; e-mail: kaisarly@dent.med.uni-muenchen.de; dkaisarly@yahoo.com

---

BM Moran, PK Ziegelmann, SB Berger, A Burey, T de Paris Matos, E Fernández, AD Loguercio, A Reis; Evaluation of Tooth Sensitivity of In-office Bleaching with Different Light Activation Sources: A Systematic Review and a Network Meta-analysis. *Oper Dent* 1 September 2021 **46(5)** E199–E223. doi: https://doi.org/10.2341/20-127-L

There are errors in the author names and contact list, in the Summary, and in the Results. The correct author spelling and author affiliations list should read (corrections are underlined):

BM Maran • PK Ziegelmann • SB Berger • A Burey • T de Paris Matos • E Fernández • AD Loguercio • A Reis

*Bianca M Maran, DDS, MS, PhD, professor, Department of Restorative Dentistry, School of Dentistry, State University of Western Paraná, Cascavel, Paraná, Brazil; Postgraduate Program in Dentistry, School of Dentistry, University of North Paraná, Londrina, Paraná, Brazil

Patrícia K Ziegelmann, DDS, MS, PhD, associate professor, Statistics Department and Post-Graduation Program in Epidemiology, Federal University of Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil

Sandrine Bittencourt Berger DDS, MS, PhD, professor, Department of Restorative Dentistry, School of Dentistry, University of North Paraná, Londrina, Paraná, Brazil

Adrieli Burey, DDS, MS, PhD, Department of Restorative Dentistry, School of Dentistry, State University of Ponta Grossa, Ponta Grossa, Paraná, Brazil

Thalita de Paris Matos, DDS, MS, assistant professor, School of Dentistry, Tuiuti University, Curitiba, Paraná, Brazil

Eduardo Fernández, DDS, MS, PhD, professor, Department Restorative Dentistry, University of Chile, Santiago de Chile, Chile; Professor, Universidad Autónoma de Chile, Instituto de Investigaciones Biomédicas, Santiago de Chile, Chile

Alessandro D Loguercio, DDS, MS, PhD, adjunct professor, Department of Restorative Dentistry, State University of Ponta Grossa, Ponta Grossa, Paraná, Brazil

Alessandra Reis, DDS, PhD, adjunctive professor, Department of Restorative Dentistry, State University of Ponta Grossa, Ponta Grossa, Paraná, Brazil

*Corresponding author: Rua Engenharia, 464 – Universitário, Cascavel, Paraná, Brazil - 85819-190; e-mail: medeiros.bianca@hotmail.com

In the Methods paragraph of the Summary:

The sentence, "A comprehensive search was performed in PubMed, Bridge Base Online (BBO), Latin American and Caribbean Health Sciences Literature database (LILACS), Cochrane Library, Scopus, Web of Science, and grey literature without date and language restrictions on April 23, 2017 (updated on September 26, 2019)."

Should read (correction is underlined):

"A comprehensive search was performed in PubMed, Bibliografia Brasileira de Odontologia (BBO), Latin American and Caribbean Health Sciences Literature database (LILACS), Cochrane Library, Scopus, Web of Science, and grey literature without date and language restrictions on April 23, 2017 (updated on September 26, 2019)."

In the Study Selection paragraph in the Results section:

The sentence, "After title screening, 227 studies remained, and this number was reduced to 32 full texts that were assessed for eligibility (Figure 1)."

Should read (correction underlined):

"After title screening, 228 studies remained, and this number was reduced to 32 full texts that were assessed for eligibility (Figure 1)."