©Operative Dentistry, 2020, **45-6,** E289-E307

Effectiveness of Whitening Strips Use Compared With Supervised Dental Bleaching: A Systematic Review and Meta-analysis

GRV da Rosa • BM Maran • VL Schmitt • AD Loguercio • A Reis • FS Naufel

Clinical Relevance

Bleaching performed at-home while under the supervision of a dentist provides greater color alteration compared with whitening strips when evaluated with a spectrophotometer, although the color alteration was undetectable by unaided human eyes.

SUMMARY

Objective: A systematic review and meta-analysis were performed to answer the following research question: Does the use of whitening strips (WS) lead to an equivalent color change compared with supervised dental bleaching in patients with permanent dentition?

Methods: A search was performed on August 10, 2017 (updated on March 22, 2019), in PubMed, the Brazilian Library in Dentistry, Latin American and Caribbean Health Sciences Literature database, Cochrane Library, Scopus, Web of Science, and grey literature, without restrictions regarding date or language. Abstracts from the International Association for Dental Research, unpublished and ongoing trial registries, dissertations, and theses were also searched. Only randomized clinical trials (parallel or split mouth) in patients with permanent dentition that compared WS with dentist-supervised dental bleaching performed at-home (AH) or in-office (IO) were included. The risk of bias (RoB) was evaluated using the Cochrane Collaboration tool. A meta-analysis with subgroup analysis (low and high peroxide concentration) was conducted for color change ΔE* (spectrophotometer) and ΔSGU (shade guide units), risk and intensity of tooth sensi-

Giulia Rechia Vasconcellos da Rosa, DDS, MS student State University of Western Paraná, Restorative Dentistry, Cascavel, Paraná, Brazil

*Bianca Medeiros Maran, DDS, MS, PhD, State University of Western Paraná, Restorative Dentistry, Cascavel, Paraná, Brazil

Vera Lucia Schmitt, DDS, MS, PhD, State University of Western Paraná, Restorative Dentistry, Cascavel, Paraná, Brazil

Alessandro D. Loguercio, DDS, MS, PhD, Department of Restortive Dentistry, State University of Ponta Grossa, Ponta Grossa, PR, Brazil

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

Fabiana Scarparo Naufel, DDS, MS, PhD, State University of Western Paraná Restorative Dentistry, Cascavel, Paraná, Brazil

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

https://doi.org/10.2341/19-160-L

tivity (TS), gingival irritation (GI), and patient satisfaction using a random effects model. Heterogeneity was assessed with the Cochran's Q test and I^2 statistics. GRADE (Grading of Recommendations, Assessment, Development and Evaluation) was used to assess the quality of the evidence.

Results: After the removal of duplicates, followed by title and abstract screening, 20 studies remained. Only two studies were considered to have a low RoB; 11 had a high RoB, and seven had an unclear RoB. For WS versus IO, data were not available for the meta-analysis. For WS versus AH bleaching, a significant difference in ΔE* favoring the AH group was observed (standardized mean difference [SMD] = −0.50, 95% confidence interval [CI] −0.79 to −0.21), but the risk (risk ratio = 0.78, 95% CI 0.65 to 0.93) and intensity of TS (SMD = −0.30, 95% CI −0.56 to −0.04) were lower in the WS group. Color change in ΔSGU, risk and intensity of GI, and patient satisfaction were not significantly different between groups ($p>0.20$). The quality of evidence for ΔE*, risk and intensity of TS, and intensity of GI were graded as moderate.

Conclusion: Although the risk and intensity of TS were lower in the WS group, dentist-supervised at-home bleaching led to a better color change when measured with a spectrophotometer, although the color alteration was undetectable by unaided human eyes.

INTRODUCTION

Nowadays, people have become more concerned about the appearance of their smile[1] and often seek out dental bleaching to improve their self-esteem, social and professional relationships, and quality of life.[2-4] A study conducted in Brazil in 2018 reported that after in-office bleaching treatment, there was a 78% increase in dental esthetic perception by patients.[5]

Although dentist-supervised bleaching is used worldwide,[6,7] limited access to dental treatment has prompted the development of over-the-counter tooth-bleaching systems in some countries, mostly known as whitening strips (WS).[8] Manufacturers claim that these products have good efficacy and lower cost, and they can be easily found online, in markets, and in pharmacies.[9] However, these unsupervised treatments can be harmful for patients in cases of abuse or use in nonindicated cases, as reported by the American Dental Association.[10] Dental bleaching also has some adverse effects, such as tooth sensitivity (TS), gingival irritation (GI),[11] and increased susceptibility to demineralization, as shown by *in vitro* studies, as well as decreased cellular viability due to the cytotoxic effects of H_2O_2.[6,12,13]

A systematic review published by Serraglio and others[14] in 2016 compared the use of over-the-counter WS vs 10% carbamide peroxide gel applied at-home using a customized tray. They concluded that there was no significant difference in color change or TS, but there was a higher rate of GI for the group treated at-home. However, some articles from previous years are missing[15-20] in this systematic review, and most of the studies included in the meta-analysis had a high risk of bias (RoB), which suggests uncertainty about the estimates provided by the authors.

Therefore, the purpose of the present systematic review of the literature was to perform a systematic review and meta-analysis to evaluate bleaching efficacy, TS, GI, and patient satisfaction with bleaching protocols performed using over-the-counter WS and dentist-supervised bleaching performed at-home or in the dentist's office. To this end, we aimed to answer the following focused research question based on the PICO acronym (Population, Intervention, Comparison, and Outcome): Does the use of over-the-counter WS lead to the same color change compared with dentist-supervised bleaching techniques in patients who undergo dental bleaching?

METHODS

Protocol and Registration

This study protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO, CRD42017070562) and followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for report.[21]

Information Sources and Search Strategy

Controlled vocabulary (MeSH terms) and free keywords were combined with the Boolean operator "OR" for the concepts "participant" and "intervention" from the PICO question addressed at the end of the Introduction section. Then, the concepts were combined with the Boolean operator "AND" to find randomized clinical trials (RCTs) that compared over-the-counter WS and dentist-supervised bleach-

Table 1: *Electronic Database and Search Strategy Conducted Initially on August 10, 2017, and Updated on March 22, 2019*

PUBMED		
#1 ((((((((((((((((((((tooth discoloration[MeSH Terms]) OR dentition, permanent[MeSH Terms]) OR colour[MeSH Terms]) OR "tooth discoloration"[Title/Abstract]) OR "tooth discolouration"[Title/Abstract]) OR "teeth discoloration"[Title/Abstract]) OR "teeth discolouration"[Title/Abstract]) OR "permanent dentition"[Title/Abstract]) OR colour[Title/Abstract]) OR colour[Title/Abstract]) OR "discoloured tooth"[Title/Abstract]) OR "discoloured tooth"[Title/Abstract]) OR "discoloured teeth"[Title/Abstract]) OR "discoloured teeth"[Title/Abstract]) OR "dental discoloration"[Title/Abstract]) OR "dental discolouration"[Title/Abstract]) OR "tooth staining"[Title/Abstract]) OR "teeth staining"[Title/Abstract]) OR "stained tooth"[Title/Abstract]) OR "stained teeth"[Title/Abstract]) OR "dental staining"[Title/Abstract])	**#2** ((((((((((((((((((((((((tooth bleaching[MeSH Terms]) OR tooth bleaching agents[MeSH Terms]) OR peroxides[MeSH Terms]) OR hydrogen peroxide[MeSH Terms]) OR self-care[MeSH Terms]) OR carbamide peroxide[Supplementary Concept]) OR non-prescription drugs[MeSH Terms]) OR bleaching[Title/Abstract]) OR peroxides[Title/Abstract]) OR "hydrogen peroxide"[Title/Abstract]) OR "carbamide peroxide"[Title/Abstract]) OR "non-prescription drugs"[Title/Abstract]) OR "self-care"[Title/Abstract]) OR whitening[Title/Abstract]) OR "in office"[Title/Abstract]) OR "at home"[Title/Abstract]) OR "over the counter"[Title/Abstract]) OR otc[Title/Abstract]) OR strips[Title/Abstract]) OR strip [Title/Abstract]) OR tray[Title/Abstract]) OR trays[Title/Abstract]) OR "pre filled" [Title/Abstract]) OR disposable	**#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])
#1 AND #2 AND #3		

ing techniques. The primary outcome evaluated was color change in ΔSGU (shade guide units) and in ΔE* (measured with a spectrophotometer colorimeter, or chromometer). The secondary outcomes were risk and intensity of TS and GI as well as patient satisfaction.

Searches were performed in MEDLINE (via PubMed), Cochrane Library, Brazilian Library in Dentistry (BBO), Latin American and Caribbean Health Sciences Literature (LILACS), as well as in the citation databases Scopus and Web of Science (Table 1) using free keywords and a controlled vocabulary (Medical Subject Heading terms [MESH]). The reference lists and the first page of linked related articles in PubMed for all primary studies were hand searched for additional relevant publications. No restrictions were placed on the publication date or language. The grey literature was investigated by searching abstracts of the annual conference of International Association for Dental Research (IADR) and its regional divisions (2001-2019), the System for Information on Grey Literature in Europe database, and dissertations and theses (ProQuest Dissertations and Thesis full-text database; Periódicos Capes thesis database).

Clinical trial registries were searched to find unpublished and ongoing trials: Current Controlled Trials (www.controlled-trials.com), the international clinical trials registry platform (http://apps.who.int/trialsearch/), ClinicalTrials.gov (www.clinicaltrials.gov), Rebec (www.rebec.gov.br), and the EU Clinical Trials Register (https://www.clinicaltrialsregister.eu).

Study Selection and Data Collection Process

We included parallel and split mouth RCTs that compared over-the-counter WS and dentist-supervised at-home and in-office bleaching techniques in patients with permanent dentition. All retrieved studies were initially scanned for relevance (according to the eligibility criteria) by title, followed by abstract reading when the title was not clear enough to check if the text met the inclusion criteria. Finally, when the abstract was not clear enough, the full texts were assessed, which were read by two reviewers. The eligible articles received a study identification (ID), combining the first author and year of publication.

Two reviewers (GRVR and BMM) independently extracted data from included articles, such as study design, participants, interventions and outcomes. In cases of disagreement, a decision was reached by consulting a third reviewer (FSN). If there were multiple reports of the same study (ie, reports with different follow-ups), data from all reports were extracted directly into a single data collection form to avoid overlapping data.

RoB in Individual Studies

Quality assessments of the selected trials were carried out by two independent reviewers, using the Risk of Bias tool from the Cochrane Collaboration.[22] The assessment criteria contained six items:

selection bias (adequate sequence generation and allocation concealment), performance bias (blinding of patient and operators), detection bias (blinding of outcome assessors), attrition bias (incomplete outcome data), reporting bias (free of selective reporting), and other possible sources of bias. Disagreements between the reviewers were solved through discussion and, if needed, by consulting a third reviewer FSN).

For each aspect of the quality assessment, the RoB was scored following the recommendations described in the Cochrane Handbook for Systematic Reviews of Interventions 5.2.0 (http://handbook.cochrane.org). Each domain level was judged as low risk, high risk, or unclear RoB. At the study level, a study was considered as low RoB if all key domains for each outcome had a low RoB. If one or more domains were judged as unclear RoB, the study was considered to have an unclear RoB. If at least one domain was considered as high RoB, the study was considered to have a high RoB.

For the outcomes of risk and intensity of TS, GI, patient satisfaction, and color change in ΔE*, adequate sequence generation and allocation concealment were the key domains. For color change in ΔSGU, blinding of outcome assessors was also considered a key domain, because the lack of blinding could affect the color measure when done with SGU. Incomplete outcome data and selective reporting were not considered key domains, as these are not problems for this type of research. Blinding of the patient and operator was not considered a key domain, because they could easily identify the different bleaching protocols.

Summary Measures and Synthesis of Results

We collected data on color change within periods ranging from immediately after to 4 weeks after bleaching. This variation was due to the differences in the assessment periods reported in the studies. When the study reported more than one follow-up, we took data from the most immediate one. Regarding TS, GI, and patient satisfaction, the worst mean value of TS reported for the group was collected.

Data were analyzed using Revman 5.3 (Review Manager version 5.3, The Cochrane Collaboration, Copenhagen, Denmark). Independent meta-analysis comparing over-the-counter WS vs at-home bleaching and over-the-counter WS vs in-office bleaching were performed in case of available data. Data from eligible studies were summarized by calculating the risk ratio (RR) along with the 95% confidence interval (CI) for the dichotomous data ratio (risk of TS and GI). For the ΔE*, ΔSGU, intensity of TS, and patient satisfaction, the mean difference (MD) was calculated when studies used the same evaluation instrument or the standardized mean difference (SMD) was employed when at least one study used a different evaluation instrument. For all meta-analyses, the random effects model was chosen to summarize the mean effect size of the primary studies. Heterogeneity was assessed using Cochran's Q test and I^2 statistics in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. The Cochran's Q test was calculated as the weighted sum of the squared differences between the individual study effects and the pooled effect across studies, with the weights being those used in the pooling method. The I^2 statistics describe the percentage of variation across studies that is due to heterogeneity rather than chance. The heterogeneity was classified as follows: $<40\%$ = low, 30% to 60% = moderate, 50% to 90% = substantial, and 75% to 100% = considerable. Overlap in the category percentages was due to the fact that other factors such as the magnitude and direction of effects as well as the strength of the evidence were taken into consideration when evaluating heterogeneity.

When more than half of the studies included in the meta-analysis did not report the standard deviation (SD), the missing data were imputed based on the average of the coefficient of variance of the remaining articles.[23]

Sensitivity analyses were conducted to investigate if assumptions made during data collection would affect the results and could be the reason for high heterogeneity, whenever detected. Analyses were also performed on studies with a high RoB.

Assessment of the Quality of Evidence Using GRADE

We graded the quality of the evidence for each outcome across studies (body of evidence) using the Grading of Recommendations: Assessment, Development and Evaluation (GRADE; http://www.gradeworkinggroup.org/) system to determine the overall strength of evidence for each outcome.[24] The GRADE approach is used to contextualize or justify intervention recommendations with four levels of evidence quality, ranging from high to very low.

For RCTs, the level of evidence is high in the GRADE approach, but it can be downgraded due to five reasons (RoB, imprecision, inconsistency, indirectness of evidence, and publication bias) in one or

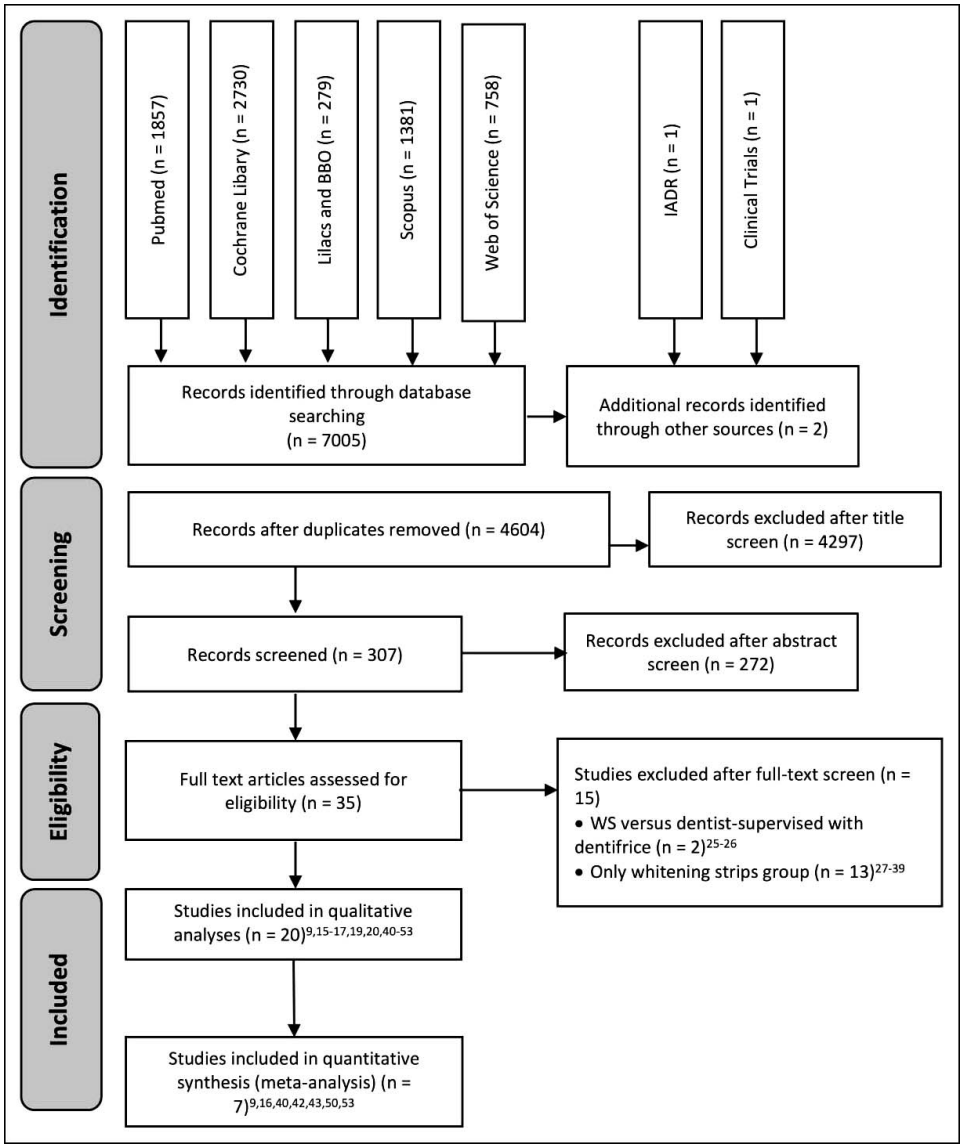

Figure 1. *Flow diagram of study identification.*

two levels. Each one of these topics was assessed as "no limitation," "serious limitations," or "very serious limitations" to allow for categorization of the quality of the evidence for each outcome into high, moderate, low, and very low. "High quality" suggests that we are very confident that the true effect lies close to the estimate of the effect. On the other extreme, "very low quality" suggests that we have very little confidence in the effect estimate, and the reported estimate can be substantially different from what was measured. The GRADEpro Guideline Development Tool, available online (www.gradepro.org), was used to create a summary of findings table, as suggested in the Cochrane Handbook for Systematic reviews of Interventions 5.2.0 (http://handbook.cochrane.org).

RESULTS

Study Selection

The search strategy was conducted initially on August 10, 2017, and was updated on March 22, 2019. After database screening and duplicate removal, 4604 studies were identified (Figure 1). After title screening, 307 studies remained, and this number was reduced to 35 studies after careful examination of the abstracts. From the 35 articles, 15 studies were excluded for the following reasons: 1) two studies compared dentist-supervised dental bleaching with dentifrice[25,26] and 2) 13 studies compared different over-the-counter WS groups.[27-39] In summary, a total of 20 studies were selected for the qualitative evaluation.

Characteristics of Included Articles

The characteristics of the 20 selected studies are listed in Table 2. The parallel study design was predominantly used in 19 studies,[9,15,17,19,20,40-53] and only one study used the split mouth design.[16]

Study Design

Eighteen studies had already been published,[9,16,17,19,40-53] and two studies were abstracts of the IADR.[15,20]

Color Evaluation Criteria

The Vita Classical shade guide (Vita Zahnfabrik, Bad Säckingen, Germany) was used in 11 studies.* Nine studies used an objective instrument for color assessment (spectrophotometer, colorimeter, or chromometer).[15,16,40-43,46,50,51] Photography was used in 11 studies† (Table 2). Four studies[16,42,43,52] used the Vita Bleachedguide 3D-Master scale (Vita Zahnfabrik, Bad Säckingen, Germany).

TS Evaluation Criteria

The intensity of self-reported TS was evaluated using a 0-10 or 0-100 visual analogue scale (VAS) in four studies,[9,42,43,50] while two studies used a 0-4[43] or 0-7[40] numeric rating scale (NRS). The risk of TS was evaluated in 15 studies.[16,17,19,41-49,51-53]

GI Evaluation Criteria

The intensity of self-reported GI was evaluated in two studies using a 0-10 VAS scale[9] or 0-7 NRS scale.[40] The risk of GI was evaluated in 15 studies.[16,17,19,41-52]

Patient Satisfaction Evaluation Criteria

Patient satisfaction was evaluated in five studies.[9,16,40,42,48]

Mean Age and Gender of the Participants in the RCTs

The mean age of all studies that reported this information was approximately 31.5 years. Five studies did not report this information[15,16,20,42,53] (Table 2). In 10 studies that reported the gender of the sample, females were more prevalent.[19,40,41,44,45,47,49-52]

* *References 9, 15, 20, 40-43, 48, 50, 51, 53.*

† *References 9, 17, 19, 40, 44, 45-49, 51.*

Bleaching Protocols

Over-the-counter WS—The product employed was hydrogen peroxide, with a concentration varying from 2.9% to 14%. In each clinical session, the product remained in contact with the dental structure from 30 to 60 minutes. The WS were used from 7 to 28 days (Table 2).

At-home bleaching—The products carbamide peroxide (10% to 35%) or hydrogen peroxide (7.5% to 10%) were employed. The bleaching trays were used from 7 to 28 days, with a daily use time that varied from 30 minutes to 10 hours (Table 2).

In-office bleaching—For in-office bleaching, hydrogen peroxide gels with concentrations that varied from 15% to 38% were employed. In each clinical session, the product remained in contact with the dental structure from 15 to 45 minutes, and one to three clinical sessions were performed.

RoB Assessment

The RoB of the eligible studies is presented in Figure 2. Ten studies were classified as high RoB in the domain sequence generation,[17,19,41,44-49,51] and one study[40] was classified at high RoB in blinding of outcome assessor during the evaluation of color in SGU. These studies were not used in the meta-analysis. The study by Aka and Celik[40] was employed in all meta-analyses, except for the outcome color change in ΔSGU.

Seven studies[17,44,45,47-49,51] were classified as having a high RoB in the domain of other possible sources due to possible conflicts of interest in the study.

Meta-analysis

All meta-analyses were performed on studies classified as at low or unclear RoB in the key domains and from which information about the outcome was reported and could be extracted. In this phase, the studies by Brito and others[15] and Rodrigues and others[20] were removed, because the data could not be extracted as they were IADR abstracts.

No study comparing WS vs IO bleaching remained at this phase. At the end, only seven studies that compared WS vs at-home bleaching were included in the meta-analysis of primary and secondary outcomes.[9,16,40,42,43,50,53]

As these studies performed different comparisons, we meta-analyzed the data in two subgroup analyses, based on the concentration of active hydrogen peroxide used in the dentist-supervised at-home

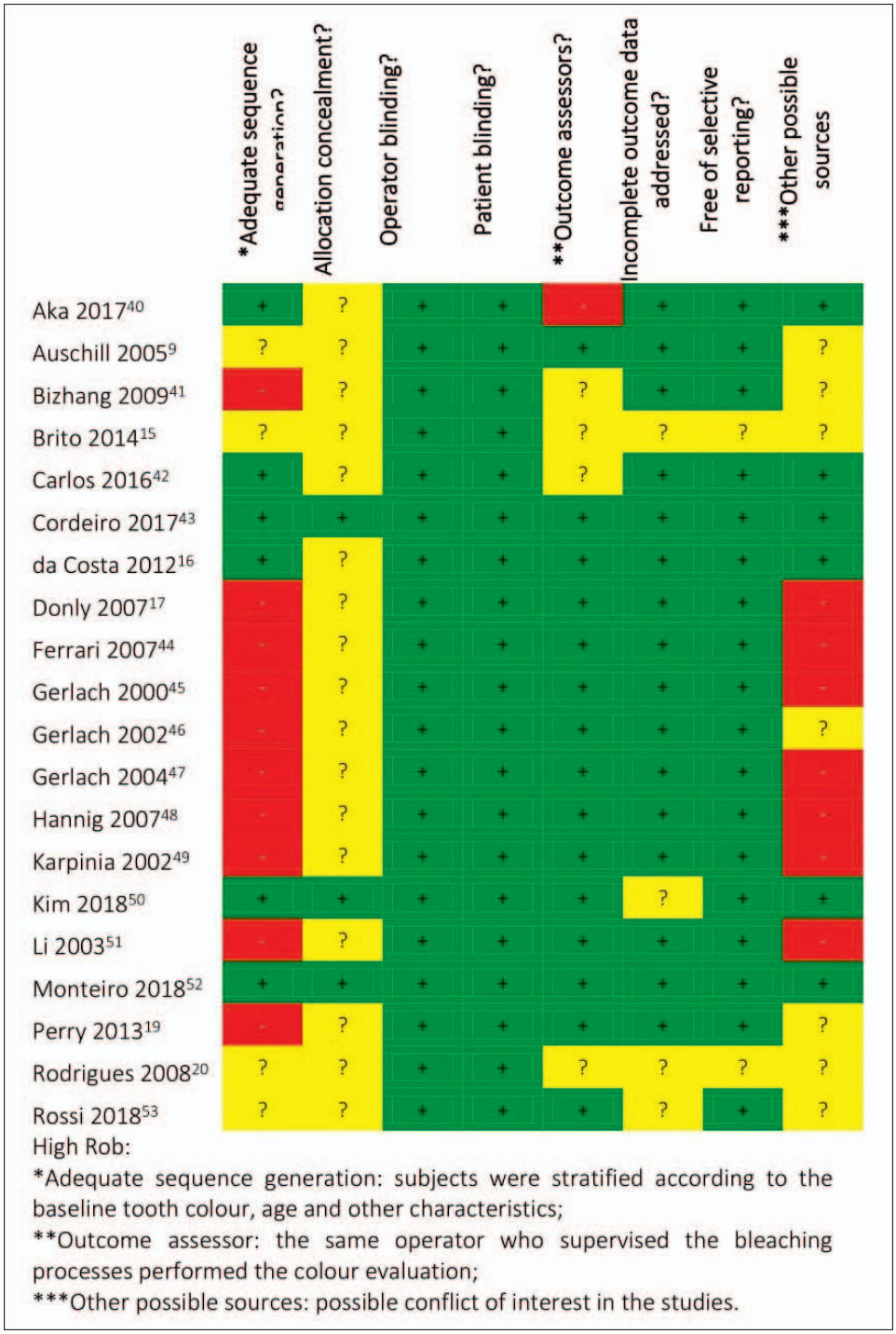

Figure 2. *Summary of the risk of bias assessment according to the Cochrane Collaboration tool.*

group. Studies that only used 10% carbamide peroxide (3.6% active hydrogen peroxide) in the dentist-supervised group were analyzed separately[9,40,42,50] from those that used a higher active hydrogen peroxide concentration (approximately 10%) in the dentist-supervised group.[16,42,43,52,53]

Color Change in ΔE* (Spectrophotometry)

Both subgroups showed that the dentist-supervised at-home group had an increase in color change (p=0.0007). The SMD was −0.50 (95% CI −0.79 to −0.21]. We did not detect heterogeneity in the data (p=0.61; I^2=0%; Figure 3).

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

Study ID	Study Design [Setting]	No. of Patients	Patient Age, Mean ± SD [Range], y	No. of Males [%]	Baseline Color/ Evaluated Tooth	Groups: Materials/No. of Patients per Group
Aka and Celik 2017[40]	Parallel [University]	92	26.0 ± n.r. [20-51]	31 [33.7]	A_1/anterior teeth	Control: no bleaching/31 AH: 10% CP[a]/30 WS: 6% HP[b]/31
Auschill and others 2005[9]	Parallel [n.r.]	39	29.8 ± n.r. [21-68]	n.r. [n.r.]	A_3/upper canine	WS: 5.3% HP[e]/13 AH: 10% CP[a]/13 IO: 38% HP[f]/13
Bizhang and others 2009[41]	Parallel [n.r.]	75	40.9 ± 14.9 [19-67]	30 [40]	A_2/anterior teeth	AH: 10% CP[g]/25 IO: 15% HP[h]/25 WS: 6% HP[e]/25
Brito and others 2014[15]	Parallel [n.r.]	36	n.r. ± n.r. [n.r.-n.r]	n.r. [n.r.]	n.r./n.r.	WS[1]: 10% HP[b]/12 IO[1]: 38% HP[f]/12 WS[2]: Strips 10% HP[b] + IO[2]: 38% HP[d]/12
Carlos and others 2016[42]	Parallel [n.r.]	75	n.r. ± n.r. [18-30]	n.r. [n.r.]	A_1/anterior teeth	WS: 10% HP[b]/25 AH[1]: 9.5% HP[j]/25 AH[2]: 10% CP[a]/25
Cordeiro and others 2017[43]	Parallel [university]	60	17.8 ± 1.44 [15-20]	n.r. [n.r.]	A_2/central incisors	AH: 10% HP[m]/20 WS[1]: 10% HP[n]/20 WS[2]: 10% HP[b]/20
da Costa and others 2012[16]	Split mouth [n.r.]	25	n.r. ± n.r. [21-75]	12 [50]	$1M_2$/anterior teeth	AH: 35% CP[a]/25 WS: 14% HP[e]/25
Donly and others 2007[17]	Parallel [n.r.]	60	14.8 ± 1.51 [12-17]	33 [55]	A_2/anterior teeth	WS: 14% HP[a]/30 AH: 10% CP[e]/30
Ferrari and others 2007[44]	Parallel [n.r.]	43	32.8 ± 11.4 [19-56]	14 [32.6]	n.r./n.r.	WS: 6% HP[e]/21 AH: 10% CP[a]/22
Gerlach and others 2000[45]	Parallel [n.r.]	36	38.4 ± 8.37 [24-57]	6 [16.7]	n.r./n.r.	WS: 5.3% HP[e]/10 AH[1]: 10% CP[a]/10 AH[2]: 15% CP[a]/11 AH[3]: 20% CP[a]/5
Gerlach and Zhou 2002[46]	Parallel [n.r.]	20	38.2 ± 10.9 [22-59]	11 [55]	n.r./n.r.	WS: 6.5% HP[e]/10 AH: 10% CP[c]/10
Gerlach and Zhou 2004[47]	Parallel [n.r.]	31	40.0 ± 12.7 [18-64]	12 [39]	A_2/anterior teeth	WS: 14% HP[e]/15 AH: 9.5% HP[p]/16
Hannig and others 2007[48]	Parallel [n.r.]	47	29.4 ± 9.00 [18-60]	25 [53.2]	A_2/anterior teeth	WS: 6% HP[e]/24 AH: 10% CP[q]/23
Karpinia and others 2002[49]	Parallel [n.r.]	69	37.2 ± 11.6 [18-65]	18 [26.1]	A_2/anterior teeth	WS: 6.5% HP[e]/35 AH: 10% CP[c]/34
Kim and others 2018[50]	Parallel [n.r.]	75	30.3 ± 5.95 [n.r.-n.r.]	11 [14.7]	n.r./n.r.	WS: 2.9% HP[r]/15 AH: 10% CP[a]/15
Li and others 2003[51]	Parallel [university]	90	42.0 ± 11.9 [23-67]	30 [33.3]	A_3/upper incisors	WS: 6.5% HP[e]/30 AH[1]: 7.5% HP[p]/30 AH[2]: 16% CP[c]/30
Monteiro and others 2018[52]	Parallel [university]	60	17.8 ± 1.44 [15-20]	24 [40]	$M_{1.5}$/central incisors	AH: 10% HP[m]/20 WS[1]: 10% HP[n]/20 WS[2]: 10% HP[b]/20

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

Study ID	Gel Protocol Daily Applications × Time, d	Conflict of Interest	Color Assessment [Outcome]	Tooth Sensitivity Scale [Outcome]	Gingival Irritation Scale [Outcome]	Patient Satisfaction Scale [Outcome]	Follow-up (days) [Drop-outs]
Aka and Celik 2017[40]	Control: no treatment AH: 1 × 10 h [14] WS: 1 × 1 h [14]	No	Vita Classical[c]; photography; spectrophtometer[d] [ΔSGU; ΔE*]	NRS 0-7 [intensity of TS]	NRS 0-7 [intensity of GI]	NRS 0-7 [intensity of PS]	10 [0] 14 [0] 30 [0] ST 180 [2]
Auschill and others 2005[9]	WS: 2 × 30 min [n.r.] AH: 1 × 8 h [n.r.] IO: 1 × 15 min [n.r.]	n.r.	Vita Classical[c]; photography [ΔSGU]	VAS 0-10 [intensity of TS]	VAS 0-10 [intensity of GI]	VAS 0-10 [intensity of PS]	7 [0]
Bizhang and others 2009[41]	AH: Overnight [14] IO: 1 × 45 min [3 sessions] WS: 2 × 30 min [14]	n.r.	Vita Classical[c]; colorimeter[j] [ΔSGU; ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	14 [0] 60 [0]
Brito and others 2014[15]	WS[1]: n.r. × n.r. [10] IO[1]: n.r. × n.r. [2 sessions] WS[2]: n.r × n.r. [10] + IO[2]: 1 × 40 min [2]	n.r.	Vita Classical[c]; spectrophtometer[n.r.] [ΔSGU; ΔE*]	VAS 0-10 [n.r.]	n.r. [n.r.]	n.r. [n.r.]	14 [n.r.] 30 [n.r.]
Carlos and others 2016[42]	WS: 1 × 30 min [14] AH[1]: 1 × 30 min [14] AH[2]: 1 × 8 h [14]	No	Vita Classical[c]; Vita 3D Master[k]; spectrophotometer[l] [ΔSGU; ΔE*]	VAS 0-10 [risk and intensity of TS]	VAS 0-10 [risk of GI]	VAS 0-10 [intensity of PS]	7 [9] 14 [9]
Cordeiro and others 2017[43]	AH: 1 × 30 min [14] WS[1 and 2]: 1 × 30 min [14]	No	Vita Classical[c]; Vita 3D Master[k]; spectrophotometer[l] [ΔSGU; ΔE*]	VAS 0-10 and NRS 0-4 [risk and intensity of TS]	VAS 0-10 [risk of GI]	n.r. [n.r.]	7 [0] 14 [0] 30 [0]
da Costa and others 2012[16]	AH: 2 × 30 min [14] WS: 2 × 30 min [14]	No	Vita 3D Master[k]; spectrophotometer[l] [ΔSGU; ΔE*]	VAS 0-10 [risk of TS]	VAS 0-10 [risk of GI]	Questionnaire [risk of PS]	15 [0] 30 [1]
Donly and others 2007[17]	WS: 2 × 30 min [14] AH: 1 × 8 h [14]	Yes	Photography; [ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	30 [2]
Ferrari and others 2007[44]	WS: 2 × 30 min [14] AH: 2 × 30 min [14]	Yes	Photography; [ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	14 [6] 30 [7]
Gerlach and others 2000[45]	WS: 2 × 30 min [14] AH[1, 2, and 3]: 1 × 2 h [14]	Yes	Photography; [ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	7 [0] 14 [4]
Gerlach and Zhou 2002[46]	WS: 2 × 30 min [14] AH: 1 × 2 h [14]	n.r.	Chromometer[i]; photography; [ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	14 [0]
Gerlach and Zhou 2004[47]	WS: 2 × 30 min [21] AH: 2 × 30 min [9]	Yes	Photography; [ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	10 [0] 22 [1]
Hannig and others 2007[48]	WS: 2 × 30 min [14] AH: 1 × 1 h [14]	Yes	Vita Classical[c]; photography; [ΔSGU; ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	Questionnaire [risk of PS]	3 [0] 7 [5] 14 [5] 60 [5]
Karpinia and others 2002[49]	WS: 2 × 30 min [21] AH: 1 × 2 h [14]	Yes	Photography; [ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	7 [2] 14 [0]
Kim and others 2018[50]	WS: 2 × 30 min [28] AH: 2 × 30 min [28]	No	Vita Classical[c]; spectrophotometer[l] [ΔSGU; ΔE*]	VAS 0-100 [intensity of TS]	NRS 0-3 [risk of GI]	n.r. [n.r.]	14 [n.r.] 28 [n.r.]
Li and others 2003[51]	WS: 2 × 30 min [21] AH: 2 × 30 min [18] AH: Overnight [21]	Yes	Vita Classical[c]; photography; chromometer[s]; [ΔSGU; ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	3 [8] 7 [8] 14 [7] 18 [7] 21 [7]
Monteiro and others 2018[52]	AH: 1 × 30 min [14] WS[1 and 2]: 1 × 30 min [14]	No	Vita 3D Master[k]; [ΔSGU]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	14 [0] 30 [0]

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

Study ID	Study Design [Setting]	No. of Patients	Patient Age, Mean ± SD [Range], y	No. of Males [%]	Baseline Color/ Evaluated Tooth	Groups: Materials/No. of Patients per Group
Perry and others 2013[19]	Parallel [dental practice]	45	37.6 ± 10.4 [18-61]	17 [38]	n.r./n.r.	WS: 9.5% HP[n.r.]/30 IO: 25% HP[n.r.]/15
Rodrigues and others 2008[20]	Parallel [n.r.]	n.r.	n.r. ± n.r. [n.r.-n.r]	n.r. [n.r.]	A_3/Anterior teeth	AH: 10% CP[f]/n.r. WS: 6.5% HP[e]/n.r.
Rossi and others 2018[53]	Parallel [university]	50	n.r. ± n.r. [18-30]	n.r. [n.r.]	A_3/anterior teeth	AH: 10% HP[m]/25 WS: 10% HP[n]/25

Abbreviations: ΔE, color difference measured with a spectrophotometer or chromometer; ΔSGU, shade guide units; AH, at-home bleaching; CP, carbamide peroxide; Dent, dental; GI, gingival irritation; HP, hydrogen peroxide; ID, identification; IO, in-office bleaching; n.r., not reported in the study; NRS, numeric rating scale; PS, patient satisfaction; SD, standard deviation; TS, tooth sensitivity; VAS, visual analogue scale; WS, whitening strips.*

Trademarks:

[a] *Opalescence PF (Ultradent Products Inc, South Jordan, UT, USA).*
[b] *Go (Ultradent Products Inc, South Jordan, UT, USA).*
[c] *Vita Classical Shade (Vita Zahnfabrik, Bad Säckingen, Germany).*
[d] *SpectroShade (MHT Optic Research AG, Niederhasli, Sweden).*
[e] *Crest Whitestrips Supreme (Oral B Procter & Gamble, Cincinnati, OH, USA).*
[f] *Opalescence Xtra Boost (Ultradent Products Inc, South Jordan, UT, USA).*
[g] *Illumine Home (Dentsply Detrey GmbH, Konstanz, Germany).*
[h] *Illumine Office (Dentsply Detrey GmbH, Konstanz, Germany).*
[i] *Chromometer ShadeEye NCC (Shofu Dental GmbH, Ratingen, Germany).*
[j] *Pola Day (SDI, Melbourne, Victoria, Australia).*
[k] *Vita Bleachedguide 3D-Master (Vita Zahnfabrik, Bad Säckingen, Germany).*
[l] *Spectrophotometer (Vita Easyshade, Vident, Brea, CA, USA).*
[m] *White Class (FGM Dental Products, Joinville, Santa Catarina, Brazil).*
[n] *3D White Strips (Oral B Procter & Gamble, Cincinnati, OH, USA).*
[°] *Nite White Excel 2 (Discus Dental Inc, Culver City, CA, USA).*
[p] *Day White Excel 3 (Discus Dental Inc, Culver City, CA, USA).*
[q] *Vivadent (Vivastyle, Schaan, Liechtenstein).*
[r] *Claren White Now strips (LG Household and Health Care, Seoul, Korea).*
[s] *Minolta CR-221 (Minolta Corporation, Ramsey, NJ, USA).*
[t] *White Perfect (FGM Dental Products, Joinville, Santa Catarina, Brazil).*

Color Change in ΔSGU

The studies by Auschill and others,[9] Carlos and others,[42] and Kim and others[50] reported the final SGU color, whereas the other two studies[43,53] reported the change from baseline. The comparison of the final measurements in an RCT, in theory, estimates the same quantity as the comparison of changes from baseline; in these cases, the outcome can be summarized in the meta-analysis only as the MD. For this reason, two studies[16,52] had to be removed from the meta-analysis, as the authors employed a different shade guide unit for color assessment (Bleachedguide), and its inclusion could only be done using the SMD (not possible in this case, as the present meta-analysis mixed final SGU measurements with change from baseline values). Thus, no significant difference was observed between the subgroups of low and high peroxide concentration (p=0.32). The MD was −0.39 (95% CI −1.16 to 0.37). We detected high heterogeneity in the overall data (p=0.0002; I^2=79%), caused by the studies that used a low hydrogen peroxide concentration (p<0.0001; I^2=91%; Figure 4).

Risk of TS

The RR was 0.78 (95% CI 0.65 to 0.93), showing significant differences between the groups (p=0.006), favoring the over-the-counter WS group. We did not detect any heterogeneity in the data (p=0.98; I^2=0%; Figure 5).

Intensity of TS

The overall SMD for the intensity of TS was −0.30 (95% CI −0.56 to −0.04) and was statistically significant (p=0.02) in favor of the over-the-counter WS group. We did not detect heterogeneity in the overall data (p=0.62; I^2=0%). The subgroup analysis revealed no significant differences between the groups (p=0.85 and p=0.13) with the low and high hydrogen peroxide concentrations, respectively (Figure 6).

Risk of GI

The RR was 0.90 (95% CI 0.40 to 2.06), showing no significant differences between the groups (p=0.81).

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

Study ID	Gel Protocol Daily Applications × Time, d	Conflict of Interest	Color Assessment [Outcome]	Tooth Sensitivity Scale [Outcome]	Gingival Irritation Scale [Outcome]	Patient Satisfaction Scale [Outcome]	Follow-up (days) [Drop-outs]
Perry and others 2013[19]	WS: 1 × 30 min [20] IO: 3 × 15 min [1]	n.r.	Photography; [ΔE*]	Questionnaire [risk of TS]	Questionnaire [risk of GI]	n.r. [n.r.]	21 [1]
Rodrigues and others 2008[20]	AH: n.r. × n.r. [21] WS: n.r. × n.r. [21]	n.r.	Vita Classical[c]; [ΔSGU]	n.r. [n.r.]	n.r. [n.r.]	n.r. [n.r.]	7 [n.r.] 14 [n.r.] 21 [n.r.] 30 [n.r.]
Rossi and others 2018[53]	AH: 2 × 30 min [7] WS: 2 × 30 min [7]	n.r.	Vita Classical[c]; [ΔSGU]	VAS 0-10 [risk of TS]	n.r.	n.r. [n.r.]	3 [n.r.] 7 [n.r.] 14 [n.r.]

We detected high heterogeneity in the data (p=0.03; I^2=71%; Figure 7).

Intensity of GI

Only two studies could be included in the subgroup[9,40] with the low peroxide concentration. The subgroup analysis revealed no significant difference between the groups (p=0.20). The SMD for the intensity of GI was 0.27 (95% CI −0.15 to 0.70; Figure 8).

Patient Satisfaction

Carlos and others[42] did not report the SD of patient satisfaction, so the SD was imputed. The SMD was −0.32 (95% CI −1.00 to 0.37), showing no significant differences between the groups (p=0.37). We detected high heterogeneity in the overall data (p=0.007; I^2=75%), caused by the studies that used a low hydrogen peroxide concentration (p = 0.004; I^2=82%; Figure 9).

Sensitivity Analysis

A meta-analysis was also performed, including studies classified at high RoB, and the results were not different (data not shown), except for the risk of TS, which in this case showed no difference between the groups.

We analyzed whether the concentration of hydrogen peroxide was responsible for the heterogeneity in the meta-analysis of color change in ΔSGU. The findings of the single study[50] that employed a low concentration of hydrogen peroxide in the over-the-counter WS group generated the heterogeneity in the aforementioned meta-analysis. Also, through a sensitivity analysis, we analyzed whether gel viscosity could cause heterogeneity in the meta-analysis of gingival irritation. The single study[42] that employed a high-viscosity gel generated the heterogeneity mentioned earlier. We also analyzed the scale used for the evaluation of patient satisfaction; a single study[40] employed a different scale (NRS 0-7) for this evaluation and was responsible for the heterogeneity in the meta-analysis.

Assessment of Evidence Quality

The body of evidence regarding color change in ΔSGU, risk of GI, and patient satisfaction was graded as very low; for this outcome, we observed that most of the RCTs were at unclear RoB, and we observed data inconsistency because of the high heterogeneity. The quality of the evidence of ΔE*, risk and intensity of TS, and intensity of GI was graded as moderate because of the unclear RoB of most articles (Table 3).

DISCUSSION

Unfortunately, many studies of this systematic review did not perform adequate sequence generation[17,19,41,44-49,51] and thus were classified as having a high RoB in this key domain. They performed random sequence by balancing patients by age, color of the teeth, or other characteristics of the patients in a nonrandom process. These articles were not included in the meta-analysis because of the lower reliability of their data.[54,55] An adequate stratification process is very important in clinical trials, because it is used to balance differences between the control and treated groups and seeks to prevent selection bias as the result of subconscious actions.[56] On the other hand, if the researchers responsible for patient recruitment have prior knowledge of the randomization of the groups, they can choose participants with a better prognosis for the experimental group and those with a worse prognosis for the control group, or vice versa.[57,58]

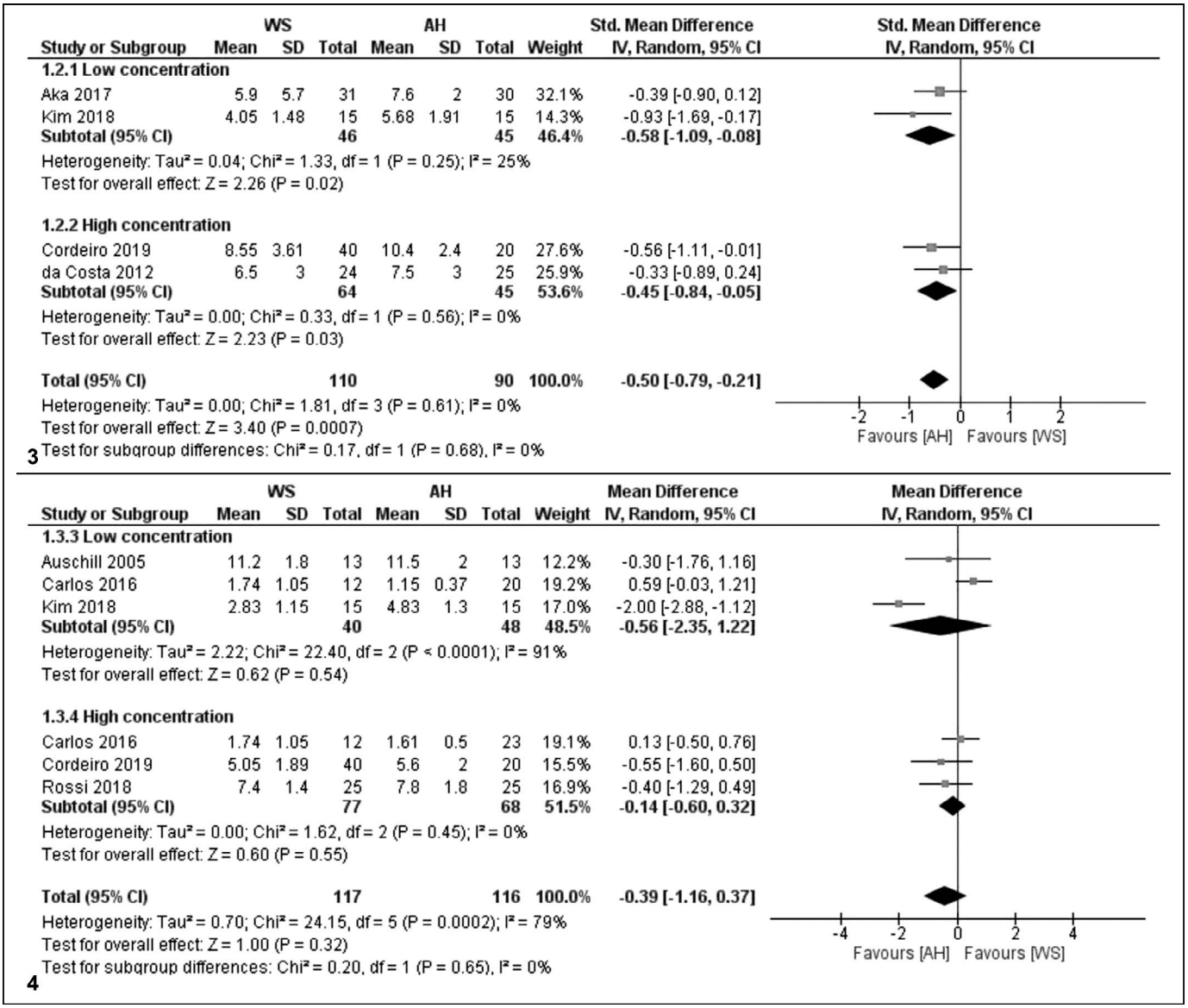

Figure 3. *Forest plot of the color change in ΔE* for WS vs AH bleaching with low and high peroxide concentrations.*

Figure 4. *Forest plot of the color change in ΔSGU for WS vs AH bleaching with low and high peroxide concentrations.*

An adequate sequence-generation process is essential for the randomization process. The authors of the most eligible studies did not reveal how the allocation concealment was performed. When inappropriately performed, larger estimates of treatment effects are observed compared with studies that had an adequate allocation concealment.[58,59]

Another important domain to reduce the RoB is the blinding of outcome assessors; because, on the contrary, the evaluator may tend to deviate from the truth because of predispositions or expectations.[60] Examiner blinding is much more important for subjective outcomes, which involve a personal judgment, for example, the assessment of color change in ΔSGU. Examiner blinding may have little practical importance when evaluators use objective tools to collect the results, such as color change in ΔE*, or for patient-centered outcomes, such as risk and intensity of TS or GI. For these latter outcomes, patient blinding is much more essential. In this way, adequate sequence generation, allocation concealment, and blinding of outcome assessors have been proposed as the most important methodological components of controlled trials.[59,61]

We also performed a meta-analysis with all eligible studies regardless of their RoB. We observed

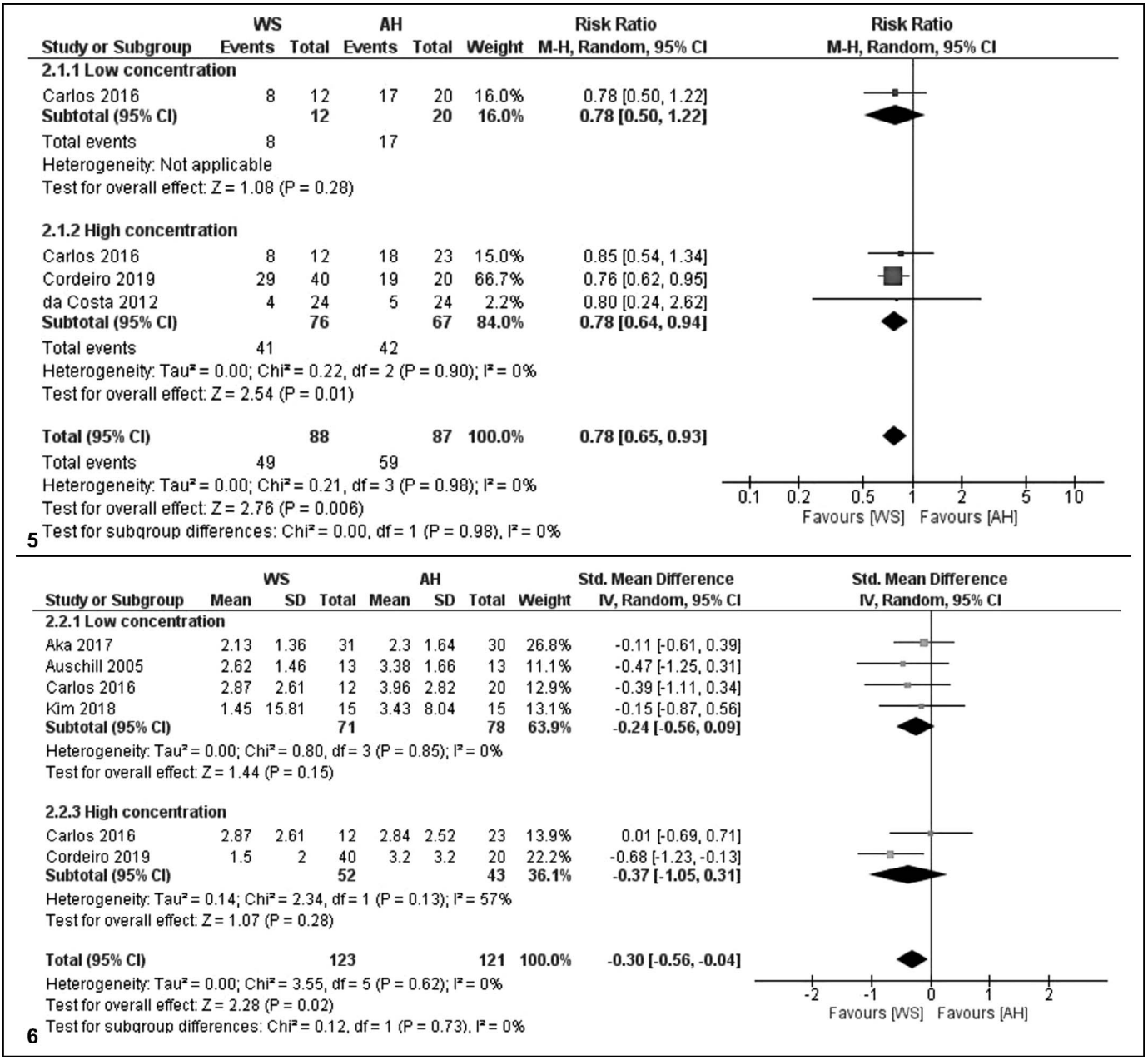

Figure 5. *Forest plot of the risk of tooth sensitivity for WS vs AH bleaching with low and high peroxide concentrations.*

Figure 6. *Forest plot of the intensity of TS for WS vs AH bleaching with low and high peroxide concentrations.*

that for all cases (except the risk of TS, which showed no difference between the groups), no differences were observed when comparing the meta-analysis of studies with a low and unclear RoB.

This study revealed a statistically significant difference in color change for ΔE* measurements in favor of dentist-supervised bleaching. The quality of the evidence for this outcome was graded as moderate, downgraded only by the fact that most RCTs had an unclear RoB. However, no significant difference in color change by ΔSGU was observed. Although the conclusions of the meta-analysis on color change in ΔE* and ΔSGU may seem contradictory, we perform a careful analysis of the SMD of −0.5 obtained for ΔE*.

Reexpressing the SMD as MD (by multiplying the SD of the control groups by the pooled SMD) resulted in an MD in ΔE* of 1 to 1.5 (taking the SD of control

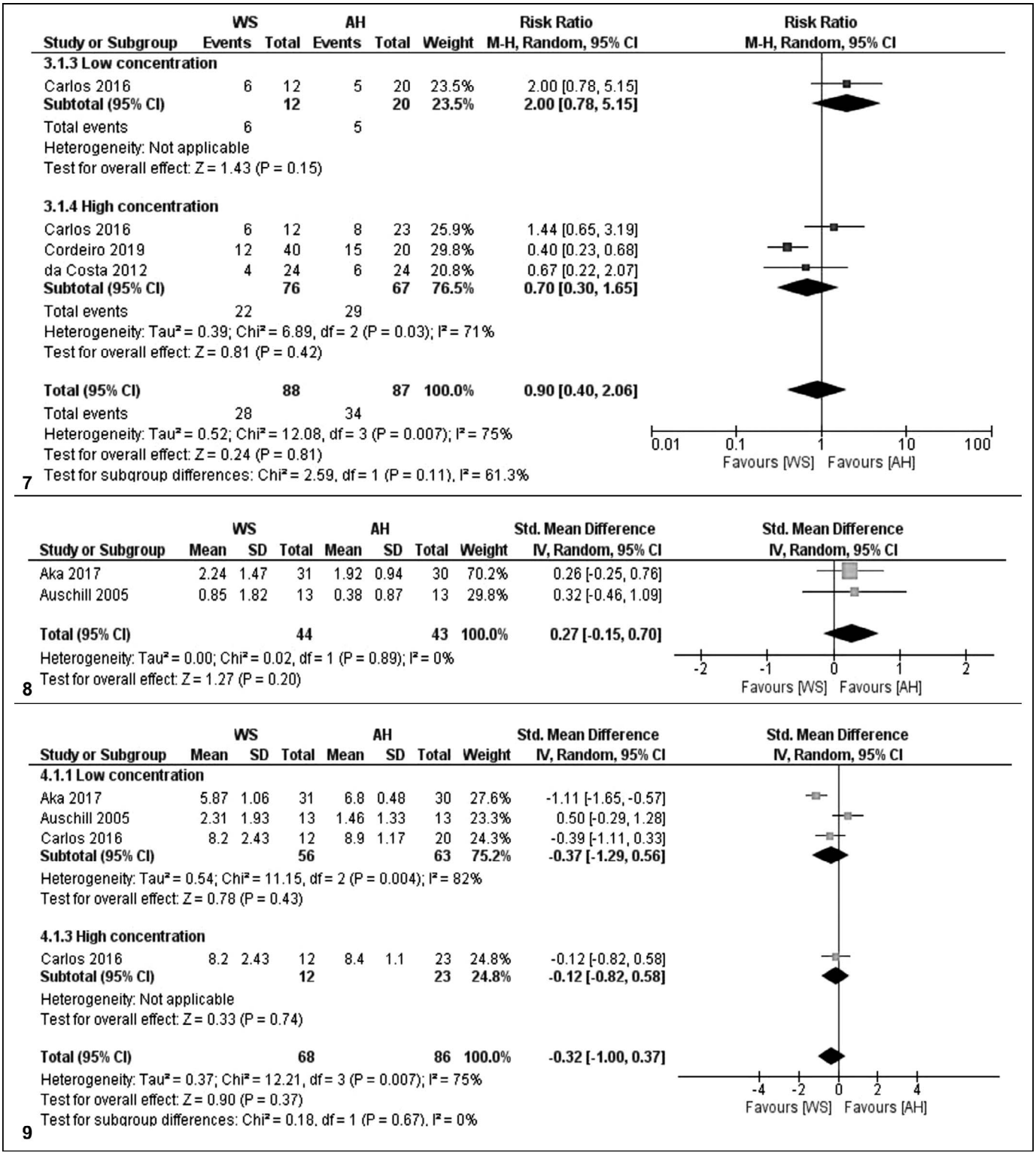

Figure 7. *Forest plot of the risk of GI for WS vs AH bleaching with high peroxide concentrations.*

Figure 8. *Forest plot of the intensity of GI for WS vs AH bleaching with low and high peroxide concentrations.*

Figure 9. *Forest plot of patient satisfaction for WS vs AH bleaching with low and high peroxide concentrations.*

Table 3: *Summary of Findings and Quality of the Evidence*[a]

Outcome	Anticipated Absolute Effects[b] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Certainty of the Evidence (GRADE)[c]
	Risk With [AH]	Risk With [WS]			
Color change in ΔE*	—	SMD 0.50 lower (0.79 lower to 0.21 lower)	—	200 (4 RCTs)	⊕⊕⊕○ MODERATE[d]
Color change in ΔSGU	The mean color change in ΔSGU was 0	MD 0.39 lower (1.16 lower to 0.37 higher)	—	233 (5 RCTs[e])	⊕○○○ VERY LOW[d,f]
Risk of TS	678 per 1.000	529 per 1.000 (441 to 631)	**RR 0.78** (0.65 to 0.93)	175 (3 RCTs[e])	⊕⊕⊕○ MODERATE[d]
Intensity of TS	The mean intensity of TS was 0	MD 0.30 lower (0.56 lower to 0.04 lower)	—	244 (5 RCTs[e])	⊕⊕⊕○ MODERATE[d]
Risk of GI	391 per 1.000	352 per 1.000 (156 to 805)	**RR 0.90** (0.40 to 2.06)	175 (3 RCTs[e])	⊕⊕○○ VERY LOW[d,f]
Intensity of GI		SMD 0.27 lower (0.15 lower to 0.70 higher)	—	87 (2 RCTs)	⊕⊕⊕○ MODERATE[d]
Patient satisfaction		SMD 0.32 lower (1.00 lower to 0.37 higher)	—	154 (3 RCTs[e])	⊕⊕○○ VERY LOW[d,f]

[a] *Only comparisons with meta-analyses were included in the table. Patient or population: [patient with dental discoloration]. Intervention: [WS]. Comparison: [AH].*
[b] *The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).*
[c] GRADE Working Group guidelines for evidence:
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, and 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, and 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, and the true effect is likely to be substantially different from the estimate of the effect.
[d] *Most RCTs are at unclear risk of bias.*
[e] *The same study was used in two subgroups.*
[f] *Inconsistency in the data due to high and unexplained heterogeneity (downgraded two levels).*

groups from eligible studies). If two objects are placed side by side in a controlled environment, the smallest difference in color detected by human observers is a ΔE* value of 1.[62] However, under clinical conditions, a ΔE* of 3.3 has been shown to be the upper limit for human eyes to detect color differences.[63]

Color matching with a shade guide scale depends on the subjective perspective of the examiner. Although this is a valid method,[64-68] with good reliability to differentiate between light and dark colors, the classical Vita shade guide is not specifically designed for dental bleaching assessments.[69,70] It is subjective to changes in the illumination of the clinical offices, weather, time of day, and season. In addition, other external factors such as observer conditions also play a role in the accuracy of color perception. However, when using devices such as chromometers or spectrophotometers, objective and precise measurements are obtained, and they are less sensitive to these sources of variation.[70] A small difference indeed exists between over-the-counter products and dentist-supervised at-home bleaching, but the pooled magnitude of color change (MD [ΔE*] = 1 to 1.5) detected in the meta-analysis can be clinically detected only by highly calibrated eyes in a controlled environment. Under clinical conditions, over-the-counter products can provide an almost equivalent color change to the dentist-supervised bleaching technique.

Regarding TS, lower sensitivity levels were observed for the over-the-counter WS group. The amount and viscosity of the product in contact with the dental substrate may account for this difference.[71] Some studies[72,73] have reported that over-the-counter WS have approximately 15% of the amount of the gel placed in customized bleaching trays. This proportion may vary depending on the dentist prescription and presence or not of reservoirs in the customized bleaching trays. The higher amount of the gel in the bleaching tray leads to a higher amount of hydrogen peroxide that reaches the pulp, causing an inflammatory reaction[74,75] and consequently increasing the risk of TS.[72,76]

Although we expected that a higher risk of GI would occur in the over-the-counter WS group because of the lack of supervision and consequent extravasation of gel into the gingival tissue,[8] no differences were detected between the groups. Under

the conditions of RCTs, patients are automatically supervised by the dentist, even when using over-the-counter products, in contrast to what happens in a clinical scenario; this may explain the similarity between the GI results.

Another important aspect is patient satisfaction after treatment, which is the main objective of dental whitening. If there is a clinically significant color change, the patient will probably be satisfied.[3] In this systematic review, there were no differences between groups.

The studies included in an earlier systematic review of the literature that addressed the same research question[14] are different from those included in the present systematic review. This earlier study included only studies that used 10% carbamide peroxide gel in the dentist-supervised at-home group, irrespective of their RoB. In addition, other recent studies have been published in the meantime that were included in the current study[16,40,42,43,50,53] but not in the earlier systematic review. These factors together explain the differences between the conclusions of the present review and the earlier one.[14]

At the moment, the Scientific Committee on Cosmetic Products and Non-Food Products recommends that tooth-whitening products should contain between 0.1% and 6.0% hydrogen peroxide, as this concentration is safe and proper if supervised by a dentist.[77] Therefore, special care should be taken for individuals with periodontal diseases, defective restorations, many fillings, crowns, and extremely dark stains. Also, conditions such as preexisting tissue injury or concurrent use of tobacco and/or alcohol may exacerbate the toxic effects of hydrogen peroxide.[78]

Finally, more studies with rigorous methodology are needed to increase the reliability of the published data.

CONCLUSIONS

Although TS was lower for the WS, dentist-supervised at-home bleaching led to a greater color change when evaluated with a spectrophotometer. However, the color alteration was undetectable by unaided human eyes.

Conflict of Interest

The authors of this article 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.

Acknowledgements

This study was partially supported by the National Council for Scientific and Technological Development (CNPq) under grants 303332/2017-4 and 308286/2019-7.

(Accepted 9 December 2019)

REFERENCES

1. Angel P, Bersezio C, Estay J, Werner A, Retamal H, Araya C, Martin J, & Fernández E (2018) Color stability, psychosocial impact, and effect on self-perception of esthetics of tooth whitening using low-concentration (6%) hydrogen peroxide *Quintessence International* **49(7)** 557-566.
2. Meireles SS, Dos Santos IDS, Della Bona Á, & Demarco FF (2009) A double-blind randomized controlled clinical trial of 10 percent versus 16 percent carbamide peroxide tooth-bleaching agents: one-year follow-up *Journal of the American Dental Association* **140(9)** 1109-1117.
3. Meireles SS, Goettems ML, Dantas RVF, Della Bona Á, Santos IS, & Demarco FF (2014) Changes in oral health related quality of life after dental bleaching in a double-blind randomized clinical trial *Journal of Dentistry* **42(2)** 114-121.
4. Bersezio C, Martín J, Angel P, Bottner J, Godoy I, Avalos F, & Fernández E (2019) Teeth whitening with 6% hydrogen peroxide and its impact on quality of life: 2 years of follow-up *Odontology* **107(1)** 118-125.
5. Soares KD, Nascimento-Júnior EM, Peixoto AC, & Silva ALF (2018) Changes in dental esthetic perceptions of patients subjected to in-office tooth bleaching *Brazilian Dental Science* **21(2)** 230-236.
6. Carey CM (2014) Tooth whitening: what we now know *Journal of Evidence-Based Dental Practice* **14** 70-76.
7. Almeida LCaGD, Soares DG, Azevedo FA, Gallinari MDO, Costa CaDS, Santos PHD, & Briso ALF (2015) At-home bleaching: color alteration, hydrogen peroxide diffusion and cytotoxicity *Brazilian Dental Journal* **26(4)** 378-383.
8. Demarco FF, Meireles SS, & Masotti AS (2009) Over-the-counter whitening agents: a concise review *Brazilian Oral Research* **23(Supplement 1)** 64-70.
9. Auschill TM, Hellwig E, Schmidale S, Sculean A, & Arweiler NB (2005) Efficacy, side-effects and patients' acceptance of different bleaching techniques (OTC, in-office, at-home) *Operative Dentistry* **30(2)** 156-163.
10. ADA Council on Scientific Affairs (2009) *Tooth Whitening/Bleaching: Treatment Considerations for Dentists and Their Patients* American Dental Association, Chicago IL.
11. Leonard RH Jr, Haywood VB, & Phillips C (1997) Risk factors for developing tooth sensitivity and gingival irritation associated with Nightguard vital bleaching *Quintessence International* **28(8)** 527-534.
12. Min K-S, Lee H-J, Kim S-H, Lee S-K, Kim H-R, Pae H-O, Chung H-T, Shin H-I, Lee S-K, & Kim E-C (2008) Hydrogen peroxide induces heme oxygenase–1 and dentin sialophosphoprotein mRNA in human pulp cells *Journal of Endodontics* **34(8)** 983-989.

13. Soares DG, Basso FG, Hebling J, & De Souza Costa CA (2014) Concentrations of and application protocols for hydrogen peroxide bleaching gels: effects on pulp cell viability and whitening efficacy *Journal of Dentistry* **42(2)** 185-198.

14. Serraglio CR, Zanella L, Dalla-Vecchia KB, & Rodrigues-Junior SA (2016) Efficacy and safety of over-the-counter whitening strips as compared to home-whitening with 10% carbamide peroxide gel—systematic review of RCTs and metanalysis *Clinical Oral Investigations* **20(1)** 1-14.

15. Brito A, Conceição E, Biondo M, Lemos G, Trevisan E, Baumgarten R, & Geribone K (2014) *Clinical Trial of New 10% Hydrogen Peroxide White Strips* Presented at the International Association for Dental Research Pan European Region Meeting, Dubrovnik, Croatia. **93(C)** 212.

16. 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.

17. Donly KJ, Segura A, Henson T, Barker ML, & Gerlach RW (2007) Randomized controlled trial of professional at-home tooth whitening in teenagers *General Dentistry* **55(7)** 669-674.

18. Li Y (2003) Tooth color measurement using chroma meter: techniques, advantages, and disadvantages *Journal of Esthetic and Restorative Dentistry* **15(Supplement 1)** S33-S41.

19. Perry R, Conde E, Farrell S, Gerlach RW, & Towers J (2013) Comparative performance of two whitening systems in a dental practice *Compendium of Continuing Education in Dentistry* **34(Special Issue 8)** 15-18.

20. Rodrigues JA, Toyoshina ER, Cassoni A, & Reis AF (2008) *Clinical Effectiveness of Over-the-Counter Bleaching Systems* Presented at the IADR/CADR General Session, Toronto, Ontario, Canada, **87(B)** 1018.

21. Moher D, Liberati A, Tetzlaff J, Altman DG, & Group P (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement *PLoS Medicine* **6(7)** e1000097.

22. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, & Sterne JA (2011) The Cochrane Collaboration's tool for assessing risk of bias in randomised trials *British Medical Journal* **343** d5928.

23. Ma J, Liu W, Hunter A, & Zhang W (2008) Performing meta-analysis with incomplete statistical information in clinical trials *BioMed Central Medical Research Methodology* **8(1)** 56.

24. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, Alonso-Coello P, Glasziou P, Jaeschke R, & Akl EA (2011) GRADE guidelines: 7. Rating the quality of evidence—inconsistency *Journal of Clinical Epidemiology* **64(12)** 1294-1302.

25. Gerlach RW, Barker ML, & Sagel PA (2001) Comparative efficacy and tolerability of two direct-to-consumer tooth whitening systems *American Journal of Dentistry* **14(5)** 267-272.

26. Karpinia K, Magnusson I, Barker ML, & Gerlach RW (2003) Clinical comparison of two self-directed bleaching systems *Journal of Prosthodontics* **12(4)** 242-248.

27. Cronin MJ, Charles CA, Zhao Q, & Dembling WZ (2005) Comparison of two over-the-counter tooth whitening products using a novel system *Compendium of Continuing Education in Dentistry* **26(2)** 140, 142, 144-148.

28. Auschill TM, Schneider-Del Savio T, Hellwig E, & Arweiler NB (2012) Randomized clinical trial of the efficacy, tolerability, and long-term color stability of two bleaching techniques: 18-month follow-up *Quintessence International* **43(8)** 683-694.

29. Collins LZ, Maggio B, Liebman J, Blanck M, Lefort S, Waterfield P, Littlewood D, Naeeni M, & Schafer F (2004) Clinical evaluation of a novel whitening gel, containing 6% hydrogen peroxide and a standard fluoride toothpaste *Journal of Dentistry* **32(Supplement 1)** 13-17.

30. Garcia-Godoy F, Villalta P, Barker ML, & Gerlach RW (2004) Placebo-controlled, 6-week clinical trial on the safety and efficacy of a low-gel, 14% hydrogen-peroxide whitening strip *Compendium of Continuing Education in Dentistry* **25(8 Supplement 2)** 21-26.

31. Gerlach RW, Zhou XJ, & McClanahan SF (2002) Comparative response of whitening strips to a low peroxide and potassium nitrate bleaching gel *American Journal of Dentistry* **15(Special Issue)** 19A-23A.

32. Gerlach RW & Sagel PA (2004) Vital bleaching with a thin peroxide gel: the safety and efficacy of a professional-strength hydrogen peroxide whitening strip *Journal of the American Dental Association* **135(1)** 98-100.

33. Gerlach RW, Barker ML, & Bagel PA (2002) Objective and subjective whitening response of two self-directed bleaching systems *American Journal of Dentistry* **15** 7A-12A.

34. Ghalili KM, Khawaled K, Rozen D, & Afsahi V (2014) Clinical study of the safety and effectiveness of a novel over-the-counter bleaching tray system *Clinical, Cosmetic and Investigational Dentistry* **6** 15-19.

35. Zantner C, Derdilopoulou F, Martus P, & Kielbassa AM (2006) Randomized clinical trial on the efficacy of 2 over-the-counter whitening systems *Quintessence International* **37(9)** 695-706.

36. Lo EC, Wong AH, & Mcgrath C (2007) A randomized controlled trial of home tooth-whitening products *American Journal of Dentistry* **20(5)** 315-318.

37. Donly KJ, Henson T, Jamison D, & Gerlach RW (2006) Clinical trial evaluating two peroxide whitening strips used by teenagers *General Dentistry* **54(2)** 110-112.

38. Donly KJ, Segura A, Sasa I, Perez E, Anastasia MK, & Farrel S (2010) A controlled clinical trial to evaluate the safety and whitening efficacy of a 9.5% hydrogen peroxide high-adhesion whitening strip in a teen population *American Journal of Dentistry* **23(5)** 292-296.

39. Donly KJ & Gerlach RW (2002) Clinical trials on the use of whitening strips in children and adolescents *General Dentistry* **50(3)** 242-245.

40. Aka B & Celik EU (2017) Evaluation of the efficacy and color stability of two different at-home bleaching systems

on teeth of different shades: a randomized controlled clinical trial *Journal of Esthetic and Restorative Dentistry* **29(5)** 325-338.

41. Bizhang M, Chun YH, Damerau K, Singh P, Raab WH, & Zimmer S (2009) Comparative clinical study of the effectiveness of three different bleaching methods *Operative Dentistry* **34(6)** 635-641.
42. Carlos N, Bridi E, Amaral F, França F, Turssi C, & Basting R (2017) Efficacy of home-use bleaching agents delivered in customized or prefilled disposable trays: a randomized clinical trial *Operative Dentistry* **42(1)** 30-40.
43. Cordeiro D, Toda C, Hanan S, Arnhold L, Reis A, Loguercio A, & Bandeira MCL (2019) Clinical evaluation of different delivery methods of at-home bleaching gels composed of 10% hydrogen peroxide *Operative Dentistry* **44(1)** 13-23.
44. Ferrari M, Cagidiaco MC, Monticelli F, Kugel G, Barker ML, & Gerlach RW (2007) Daytime use of a custom bleaching tray or whitening strips: initial and sustained color improvement *American Journal of Dentistry* **20** 19A-22A.
45. Gerlach RW, Gibb RD, & Sagel PA (2000) A randomized clinical trial comparing a novel 5.3% hydrogen peroxide whitening strip to 10%, 15%, and 20% carbamide peroxide tray-based bleaching systems *Compendium of Continuing Education in Dentistry* **29** S22-S28.
46. Gerlach RW & Zhou X (2002) Comparative clinical efficacy of two professional bleaching systems *Compendium of Continuing Education in Dentistry* **23(1A)** 35-41.
47. Gerlach RW & Zhou X (2004) Clinical trial comparing two daytime hydrogen-peroxide professional vital-bleaching systems *Compendium of Continuing Education in Dentistry* 25**(8 Supplement 2)** 33-40.
48. Hannig C, Lindner D, & Attin T (2007) Efficacy and tolerability of two home bleaching systems having different peroxide delivery *Clinical Oral Investigations* **11(4)** 321-329.
49. Karpinia KA, Magnusson I, Sagel PA, Zhou X, & Gerlach RW (2002) Vital bleaching with two at-home professional systems *American Journal of Dentistry* **15(Special Issue)** 13A-18A.
50. Kim Y, Ha A, Kim J, & Kim S (2018) Double-blind randomized study to evaluate the safety and efficacy of over-the-counter tooth-whitening agents containing 2.9% hydrogen peroxide *Operative Dentistry* **43(3)** 272-281.
51. Li Y, Lee SS, Cartwright SL, & Wilson AC (2003) Comparison of clinical efficacy and safety of three professional at-home tooth whitening systems *Compendium of Continuing Education in Dentistry* **24(5)** 357-360, 362, 364.
52. Monteiro MJF, Lindoso JBC, De Oliveira Conde NC, Da Silva LM, Loguercio AD, & Pereira JV (2018) Evaluation of the genotoxic potential of different delivery methods of at-home bleaching gels: a single-blind, randomized clinical trial *Clinical Oral Investigations* **23(5)** 2199-2206.
53. Rossi B, Freitas P, Tedesco T, Gonçalves F, & Ferreira L (2018) Tooth color changes and sensitivity in patients undergoing dental bleaching with 10% hydrogen peroxide using customized trays or strips: a randomized clinical trial *Minerva Stomatologica* **67(2)** 55-61.
54. Viswanathan M, Patnode CD, Berkman ND, Bass EB, Chang S, Hartling L, Murad MH, Treadwell JR, & Kane RL (2017) Assessing the risk of bias in systematic reviews of health care interventions In: *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* Agency for Healthcare Research and Quality, Rockville, MD.
55. Hartling L, Hamm MP, Milne A, Vandermeer B, Santaguida PL, Ansari M, Tsertsvadze A, Hempel S, Shekelle P, & Dryden DM (2013) Testing the risk of bias tool showed low reliability between individual reviewers and across consensus assessments of reviewer pairs *Journal of Clinical Epidemiology* **66(9)** 973-981.
56. D'agostino RB (1998) Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group *Statistics in Medicine* **17(19)** 2265-2281.
57. Schulz KF, Chalmers I, Grimes DA, & Altman DG (1994) Assessing the quality of randomization from reports of controlled trials published in obstetrics and gynecology journals *Journal of the American Medical Association* **272(2)** 125-128.
58. Odgaard-Jensen J, Vist GE, Timmer A, Kunz R, Akl EA, Schünemann H, Briel M, Nordmann AJ, Pregno S, & Oxman AD (2011) Randomisation to protect against selection bias in healthcare trials *Cochrane Database of Systematic Reviews* **(4)** MR00012.
59. Schulz KF (1995) Subverting randomization in controlled trials *Journal of the American Medical Association* **274(18)** 1456-1458.
60. Hróbjartsson A, Thomsen ASS, Emanuelsson F, Tendal B, Hilden J, Boutron I, Ravaud P, & Brorson S (2012) Observer bias in randomised clinical trials with binary outcomes: systematic review of trials with both blinded and non-blinded outcome assessors *British Medical Journal* **344** e1119.
61. Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, Dickersin K, Hróbjartsson A, Schulz KF, & Parulekar WR (2013) SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials *British Medical Journal* **346** e7586.
62. Kuehni RG & Marcus RT (1979) An experiment in visual scaling of small color differences *Color Research & Application* **4(2)** 83-91.
63. Ruyter I, Nilner K, & Möller B (1987) Color stability of dental composite resin materials for crown and bridge veneers *Dental Materials* **3(5)** 246-251.
64. Marson FC, Sensi LG, Vieira LCC, & Araujo E (2008) Clinical evaluation of in-off ice dental bleaching treatments with and without the use of light-activation sources *Operative Dentistry* **33(1)** 15-22.
65. Maran BM, Vochikovski L, De Andrade Hortkoff DR, Stanislawczuk R, Loguercio AD, & Reis A (2018) Tooth sensitivity with a desensitizing-containing at-home bleaching gel: a randomized triple-blind clinical trial *Journal of Dentistry* **72** 64-70.

66. 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.

67. 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.

68. 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.

69. Paravina RD, Johnston WM, & Powers JM (2007) New shade guide for evaluation of tooth whitening—colorimetric study *Journal of Esthetic and Restorative Dentsitry* **19(5)** 276-283.

70. Meireles SS, Demarco FF, Santos IS, Dumith SC, & Bona AD (2008) Validation and reliability of visual assessment with a shade guide for tooth-color classification *Operative Dentistry* **33(2)** 121-126.

71. Kwon SR, Li Y, Oyoyo U, & Aprecio RM (2012) Dynamic model of hydrogen peroxide diffusion kinetics into the pulp cavity *Journal of Contemporary Dental Practice* **13(4)** 440-445.

72. Dahl J & Becher R (1995) Acute toxicity of carbamide peroxide and a commercially available tooth-bleaching agent in rats *Journal of Dental Research* **74(2)** 710-714.

73. Haywood VB & Robinson FG (1997) Vital tooth bleaching with Nightguard vital bleaching *Current Opinion in Cosmetic Dentistry* **4** 45-52.

74. De Souza Costa CA, Riehl H, Kina JF, Sacono NT, & Hebling J (2010) Human pulp responses to in-office tooth bleaching *Oral Surgery, Oral Medicin, Oral Pathology, Oral Radiology, and Endodontics* **109(4)** e59-e64.

75. Caviedes-Bucheli J, Ariza-García G, Restrepo-Méndez S, Ríos-Osorio N, Lombana N, & Muñoz HR (2008) The effect of tooth bleaching on substance P expression in human dental pulp *Journal of Endodontics* **34(12)** 1462-1465.

76. Roderjan DA, Stanislawczuk R, Hebling J, Costa CaDS, Reis A, & Loguercio AD (2015) Response of human pulps to different in-office bleaching techniques: preliminary findings *Brazilian Dental Journal* **26(3)** 242-248.

77. Commission E (2003) Opinion of the Scientific Committee on Cosmetic Products and Non-food Products intended for consumers concerning hydroxyisohexyl 3-cyclohexene carboxaldehyde Presented at the 26th Plenary Meeting of the SCCNFP.

78. Lima SNL, Ribeiro IS, Grisotto MA, Fernandes ES, Hass V, De Jesus Tavarez RR, Pinto SCS, Lima DM, Loguercio AD, & Bandeca MC (2017) Evaluation of several clinical parameters after bleaching with hydrogen peroxide at different concentrations: a randomized clinical trial *Journal of Dentistry* **68** 91-97.

qualifications/experience. Learn more and/or apply at Jobs@UIowa at: https://jobs.uiowa.edu/faculty/view/74051, reference Req #74051. The University of Iowa is an equal opportunity/affirmative action employer. All qualified applicants are encouraged to apply and will receive consideration for employment free from discrimination on the basis of race, creed, color, national origin, age, sex, pregnancy, sexual orientation, gender identity, genetic information, religion, associational preference, status as a qualified individual with a disability, or status as a protected veteran.

Errata:

Operative Dentistry apologizes for the layout and clarity errors in the manuscripts, "Time-dependent Microhardness Gradients of Self-adhesive Resin Cements Under Dual- and Self-curing Modes", and "Effectiveness of Whitening Strips Use Compared With Supervised Dental Bleaching: A Systematic Review and Meta-analysis" published as online only articles attached to volume 45 issue 61.

Both articles were published without the final proof corrections being made. In both cases, the corrections to be made were only for style and readability and do not impact the science represented in the article.

The articles have been corrected and reposted to the website.

Our apologies to the authors and our readers for publishing content that was formatted below our standards.

The two articles affected are:

GRV da Rosa, BM Maran, VL Schmitt, AD Loguercio, A Reis, FS Naufel; Effectiveness of Whitening Strips Use Compared With Supervised Dental Bleaching: A Systematic Review and Meta-analysis. Oper Dent 1 November 2020; 45 (6): E289–E307. doi: https://doi.org/10.2341/19-160-L

T Geng, Y Pan, Z Liu, C Yuan, P Wang, X Meng; Time-dependent Microhardness Gradients of Self-adhesive Resin Cements Under Dual- and Self-curing Modes. Oper Dent 1 November 2020; 45 (6): E280–E288. doi: https://doi.org/10.2341/19-006-L