Clinical Oral Investigations (2024) 28:679
https://doi.org/10.1007/s00784-024-06036-z

REVIEW

# Effect of the reduction in the exposure time to at-home bleaching gel on color change and tooth sensitivity: A systematic review and meta-analysis

**Priscila Borges Gobbo de Melo[1] · Letícia Vasconcelos Silva Souza[1] · Lucianne Cople Maia[2] · Guido Artemio Marañón-Vásquez[3] · Matheus Kury[4] · Vanessa Cavalli[1]**

Received: 6 September 2024 / Accepted: 4 November 2024


## Abstract

**Objective** To investigate the effect of reducing exposure time to at-home bleaching gel on color change and tooth sensitivity.

**Materials and methods** The search was carried out using PubMed, Scopus, Web of Science, EMBASE, LILACS, Cochrane. Randomized clinical trials (RCTs) were included involving adult patients who have never undergone bleaching treatment before (P), subjected to bleaching with a reduced exposure time to the at-home bleaching agent (I) compared to those who used it for the time indicated by the manufacturer (C), to evaluate the effects on color change and tooth sensitivity (O). The Cochrane guidelines for the Risk of Bias Assessment Tool (RoB 2.0) and GRADE were used to assess risk of bias and quality of evidence, respectively.

**Results** Using at-home bleaching gel for the period recommended by the manufacturer resulted in significantly higher $\Delta E_{ab}$ and $\Delta WI_D$ values and better subjective color change (ΔSGU—Classical), regardless of the evaluation time. Regarding the post-bleaching evaluation, no significant differences were found for $\Delta E_{00}$ immediately after bleaching or ΔSGU (Bleached) at any time. Reducing the time of use significantly decreased tooth sensitivity events.

**Conclusions** Reducing exposure time to at-home bleaching gel reduces tooth sensitivity events; however, most of the parameters that assess color change indicate using at-home bleaching gel for the time recommended by the manufacturer.

**Clinical significance** Reducing exposure time to at-home bleaching gel should be applied with caution in clinical practice. Although the evidence suggests a reduction in tooth sensitivity events, bleaching effectiveness was significantly higher after using the bleaching gel for the time indicated by the manufacturer.

**Keywords** Tooth bleaching · Bleaching agents · Tooth sensitivity · Time

✉ Vanessa Cavalli
cavalli@unicamp.br

Priscila Borges Gobbo de Melo
pribgobbo@gmail.com

Letícia Vasconcelos Silva Souza
s.vasconcelosleticia@gmail.com

Lucianne Cople Maia
maia_lc@ufrj.b

Guido Artemio Marañón-Vásquez
guido_amv@hotmail.com

Matheus Kury
matheuskury@hotmail.com

[1] Department of Restorative Dentistry, Piracicaba Dental School, University of Campinas, 901 Limeira Avenue, Areião, Piracicaba, SP 13414-903, Brazil

[2] Department of Pediatric Dentistry and Orthodontics, School of Dentistry, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

[3] Department of Pediatric Dentistry, School of Dentistry of Ribeirao Preto, University of São Paulo, Ribeirão Preto, SP, Brazil

[4] Dental Research Division, School of Dentistry, Paulista University (UNIP), São Paulo, SP, Brazil

Published online: 03 December 2024

## Introduction

The aesthetic appearance of teeth has played an essential role in modern society, where people associate it with self-esteem and social acceptance [1]. In this context, the increasing demand for tooth bleaching reflects not only the desire for a better quality of life, but also the standards of beauty imposed by society [2–6]. Tooth bleaching effectively addresses dental discoloration and is a popular approach based on its cost-effectiveness and less invasive alternative to restorative procedures [7, 8]. The treatment involves applying high- or low-concentration peroxide gels to the buccal surface of the enamel, which would be capable of diffusing towards the dentin. When in contact with water, the hydrogen peroxide is decomposed into oxygen free radicals (ROS) that break down dental chromophores (pigments) into shorter molecules [9–11].

Among the bleaching techniques and materials available for its performance, in-office bleaching uses high concentrations (25–40%) of hydrogen (HP) or carbamide peroxide (CP) [12]. On the other hand, at-home tooth bleaching is based on the use of personalized bleaching trays loaded daily by the patient with low concentrations of HP and CP (< 10% and 22%, respectively) [7, 13, 14]. Regardless of the technique and products employed, bleaching effectiveness is reported for most cases when the procedure is performed correctly, according to the clinical indication [14].

Tooth sensitivity remains a common adverse effect associated with bleaching treatments. Still, a systematic review and meta-analysis showed that less concentrated CP gels when compared to more concentrated gels, may cause less risk and intensity of tooth sensitivity during at-home bleaching [14]. However, these lower-concentration gels generally require longer application times to achieve satisfactory aesthetic outcomes. In this context, some researchers have shown that reducing the application time may not negatively affect the efficacy of at-home bleaching, thereby increasing patient comfort without compromising the esthetic outcomes [1, 15]. In addition, it is possible to reduce the time needed for bleaching by employing low-concentration HP gels for at-home treatment [15]. Although the manufacturer recommends using the bleaching gel (HP 4%) for 2 h a day, one study showed that after 60 min, over two-thirds of the HP was consumed [16], and the amount of gel that reacts with the tooth decreases by half after twenty minutes [17]. Thus, using the tray within the time indicated by the manufacturer can still be overestimated [17].

Randomized clinical trials (RCTs) have evaluated whether reducing the daily time of wearing the individual tray during at-home bleaching treatment influenced the bleaching efficacy and tooth sensitivity [1, 15, 17, 18]. Although these clinical studies provide valuable insights individually, there is currently no systematic review and meta-analysis that comprehensively synthesizes these findings. Such analysis is essential for a robust assessment of the overall evidence, clarifying the effects of reduced exposure times of at-home bleaching gels on color change and sensitivity across different studies. Therefore, this systematic review with meta-analysis aims to fill this gap by answering the question: Does the reduced time of use of at-home bleaching gel (I) influence the color change and tooth sensitivity (O) in adults (P) when compared to the use for the time indicated by the manufacturer (C)?

## Material and methods

### Protocol and registration

This study was registered in the International Prospective Register of Systematic Reviews (PROSPERO – CRD42022324330). Furthermore, this systematic review followed the guidelines laid out in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement to be reported [19].

### Eligibility criteria

The eligibility criteria were defined based on the following PICOS strategy:

1. **Participant (P):** Adult patients with no dental caries, no need for endodontics, orthodontics, or periodontal treatment, and who have never undergone bleaching treatment before;
2. **Intervention (I):** Reduced exposure time to the at-home bleaching agent;
3. **Comparison (C):** Exposure time to the at-home bleaching agent indicated by the manufacturer;
4. **Outcome (O):** Color change in shade guide units (ΔSGU) and with a spectrophotometer/colorimeter/chromameter (ΔE*, CIEL*a*b* or CIEDE2000 and Whiteness Index, $\Delta WI_D$) and tooth sensitivity (relative risk, RR);
5. **Study design (S):** Randomized controlled trials (RCT).

Only parallel or split-mouth randomized controlled trials (RCTs) were included in this systematic review. Thus, the exclusion criteria were as follows: reviews, case reports, *in situ* studies, *in vitro* studies, studies using participants with deciduous teeth, and studies that did not evaluate at least two groups (intervention and comparison) and others that compared bleaching results in non-vital teeth.

The selected studies were chosen for their direct relevance to the field. They evaluated groups that used an at-home bleaching technique, using an individual tray with low-concentrated bleaching gels (HP or CP). The studies were expected to have evaluated the efficacy and tooth sensitivity caused by the gels in two distinct time regimens: the time recommended by the manufacturer and a reduced one.

## Information sources and search strategy

The controlled vocabulary (MeSH terms), synonyms, and free keywords were combined with the Boolean operators "AND" and "OR" and then, the search strategy was defined for the MEDLINE database by PubMed and adapted to other electronic databases (Scopus, Web of Science, EMBASE, LILACS—via VHL and Cochrane) (Table 1). The gray literature was explored by searching abstracts at the International Association of Dental Research (IADR) annual conference, studies in Data Archiving and Networked Services (DANS), and Google Scholar (one hundred first references). Dissertations and theses were searched in the Bases of Dissertations and Periodic Theses of ProQuest at Capes and the ongoing studies in the following clinical trial registries: ClinicalTrials.gov (www.ClinicalTrials.gov) and Brazilian Registry of Clinical Trials (www.rebec.gov.br). No restrictions were applied regarding language, publication date, or any other filters during the database searches to avoid limiting the studies retrieved. Randomized parallel and split-mouth clinical trials RCTs that compared the reduced use time of at-home bleaching gel *versus* the time indicated by the manufacturer in adult patients with permanent dentition were included.

## Study selection and data collection process

All the studies found were exported to reference management software (Endnote™), and duplicate citations were removed by two independent reviewers (PBGM and LV). After that, the studies were screened. These screened studies were then included in the Rayyan™ platform to determine their relevance based on their titles. Subsequently, the studies were evaluated to decide whether to read the full text. It was read entirely if a study had insufficient information in the title or abstract. The same two reviewers then read the selected articles to identify if they met the inclusion criteria. A third reviewer (MK) was consulted in case of any disagreement. The two reviewers (PBGM and LV) performed data extraction independently, collecting information about the details of each study (author and year), study design (parallel or split-mouth), the number of participants (per group and total), the average age of the participants, the interventions carried out, and the parameters used (color and sensitivity analysis). The results of the analyzed parameters were summarized. When data were not reported in studies, authors were contacted by email to request missing information.

## Risk of *bias* in individual studies

The two reviewers (PBGM and LV) independently assessed the individual quality of the selected studies through the risk of bias using Cochrane instruments. The risk of bias in RCTs was analyzed with the Cochrane Risk of Bias Assessment Tool (RoB 2.0) [20], which evaluates bias across five domains:

(1) Bias arising from the randomization process;
(2) Bias due to deviations from intended interventions;
(3) Bias due to missing outcome data;
(4) Bias in measurement of the outcome;
(5) Bias in selection of the reported results.

Each domain was judged as having either low risk of bias, some concerns, or high risk of bias based on possible answers: yes, probably yes, probably no, no, not applicable, and no information. For a study to be considered low risk, it needed to receive low risk grades in all domains. Studies with low risk of bias in some domains and some concerns in others were classified as having some concerns. Additionally, if one domain was judged to have a serious or critical risk of bias, the study was classified as having a serious risk of bias.

## Synthesis methods

The meta-analysis of all data was conducted using the statistical software Revman 5 (Review Manager version 5.4). Data on color change measured with different units of color scale were not associated. Thus, for the different continuous outcomes, the mean difference (MD) was utilized and meta-analyses were carried out regarding 1- Color change through the CIEL*a*b* system ($\Delta E_{ab}$), 2- Color change through the CIEDE 2000 system ($\Delta E_{00}$), 3- Whitening index ($\Delta WI_D$), 4- Color change through the classical shade guide system (ΔSGU-Classical), and 5- Color change through the shade guide system for bleached teeth (ΔSGU-Bleached). For all outcomes, the meta-analysis was performed at 2 different time points: 1st: after 2 weeks from the beginning of the bleaching treatment, and 2nd: after 1 week from the end of the bleaching treatment (considered short-term, follow-up). For the dichotomous outcome (tooth sensitivity), RR data were used.

The analyses included methodologically and clinically homogeneous studies. Meta-analyses were carried out by combining both evaluated bleaching agents, hydrogen

**Table 1** Search strategies by electronic database

| | | |
|---|---|---|
| Pubmed | | |
| **#1** ("tooth bleaching agents"[MeSH] OR "tooth bleaching"[MeSH] OR "carbamide peroxide"[MeSH] OR "hydrogen peroxide"[MeSH] OR "bleaching"[Tiab] OR "whitening"[Tiab] OR "Carbamide peroxide"[Tiab] OR "Hydrogen peroxide"[Tiab])<br>#1 AND #2 AND #3 | **#2** (Color[MeSH] OR Color[Tiab] OR Spectrophotometry[MeSH] OR Spectrophotometry[Tiab] OR "Shade change"[Tiab] OR "easy shade"[Tiab] OR "Visual Analog Scale"[MeSH] OR "Visual analog scale"[Tiab] OR "vita classical"[Tiab] OR "Numerical rating scale"[Tiab] OR "Tooth Sensitivity"[Tiab] OR "Teeth sensitivity"[Tiab] OR "Dental sensitivity"[Tiab] OR "Sensitivity risk"[Tiab]) | **#3** (time[MeSH] OR time*[Tiab]) |
| Scopus | | |
| **#1** INDEXTERMS ( {tooth bleaching agents} OR {tooth bleaching} OR {carbamide peroxide} OR {hydrogen peroxide}) OR TITLE-ABS ( {bleaching} OR {whitening} OR{Carbamide peroxide} OR {Hydrogen peroxide})<br>#1 AND #2 AND #3 | **#2** INDEXTERMS ( {Color} OR {Spectrophotometry} OR {Visual Analog Scale}) OR TITLE-ABS ( {Color} OR {Spectrophotometry} OR {Shade change} OR {easy shade} OR {Vita classical} OR {Visual analog scale} OR {Numerical rating scale} OR {Tooth Sensitivity} OR {Teeth sensitivity} OR {Dental sensitivity} OR {Sensitivity risk}) | **#3** INDEXTERMS ( {time}) OR TITLE-ABS ( {time} OR {times}) |
| Cochrane Library | | |
| **#1** MeSH descriptor: [Tooth Bleaching Agents] explode all trees<br>**#2** MeSH descriptor: [Tooth Bleaching] explode all trees<br>**#3** MeSH descriptor: [Carbamide Peroxide] explode all trees<br>**#4** MeSH descriptor: [Hydrogen Peroxide] explode all trees<br>**#5** ("bleaching" OR "whitening" OR "Carbamide peroxide" OR "Hydrogen peroxide"):ti,ab,kw<br>**#6** — **#1** OR #2 OR #3 OR #4 OR #5<br>**#7** MeSH descriptor: [Color] explode all | **#7** MeSH descriptor: [Color] explode all trees<br>**#8** MeSH descriptor: [Spectrophotometry] explode all trees<br>**#9** MeSH descriptor: [Visual Analog Scale] explode all trees<br>**#10** ("Color" OR "Spectrophotometry" OR "Shade change" OR "easy shade" OR "Vita classical" OR "Visual analog scale" OR "Numerical rating scale" OR "Tooth Sensitivity" OR "Teeth sensitivity" OR "Dental sensitivity" OR "Sensitivity risk"):ti,ab,kw | **#11** — #7 OR #8 OR #9 OR #10<br>**#12** MeSH descriptor: [Time] explode all trees<br>**#13** (time*):ti,ab,kw<br>**#14** — #12 OR #13<br>**#15** — #6 AND #11 AND |
| Web of Science | | |
| **#1** TS = ("bleaching" OR "whitening" OR "Carbamide peroxide" OR "Hydrogen peroxide")<br>#1 AND #2 AND #3 | **#2** TS = ("Color" OR "Spectrophotometry" OR "Visual analog scale" OR "vita classical" OR "Shade change" OR "easy shade" OR "Numerical rating scale" OR "Tooth Sensitivity" OR "Teeth sensitivity" OR "Dental sensitivity" OR "Sensitivity risk") | **# 3** TS = ("time*") |
| Lilacs via VHL | | |
| **#1** tw:(tw:("bleaching" OR "whitening" OR "Carbamide peroxide" OR "Hydrogen peroxide") OR ( mh:("Tooth Bleaching Agents" OR "Tooth Bleaching" OR "Carbamide Peroxide" OR "Hydrogen Peroxide")))<br>#1 AND #2 AND #3 | **#2** tw:(tw:("color" OR "spectrophotometry" OR "Visual analog scale" OR "vita classical" OR "Shade change" OR "easy shade" OR "Numerical rating scale" OR "Tooth Sensitivity" OR "Teeth sensitivity" OR "Dental sensitivity" OR "Sensitivity risk") OR ( mh:("Color" OR "Spectrophotometry" OR "Visual analog scale"))) | **#3** tw:(tw:("time*") OR ( mh:("Time"))) AND ( db:("LILACS")) |
| Embase | | |
| **#1** 'tooth bleaching agent'/exp OR 'carbamide peroxide'/exp OR 'hydrogen peroxide'/exp<br>**#2** 'tooth bleaching agent':ti,ab,kw OR 'bleaching':ti,ab,kw OR 'whitening':ti,ab,kw OR 'carbamide peroxide':ti,ab,kw OR 'hydrogen peroxide':ti,ab,kw<br>**#3** — #1 OR #2 | **#4** 'color'/exp OR 'spectrophotometry'/exp OR 'visual analog scale'/exp<br>**#5** 'color':ti,ab,kw OR 'spectrophotometry':ti,ab,kw OR 'shade change':ti,ab,kw OR 'easy shade':ti,ab,kw OR 'vita classical':ti,ab,kw OR 'visual analog scale':ti,ab,kw OR 'numerical rating scale':ti,ab,kw OR 'tooth sensitivity':ti,ab,kw OR 'teeth sensitivity':ti,ab,kw OR 'dental sensitivity':ti,ab,kw OR 'sensitivity risk':ti,ab,kw | **#6** — #4 OR #5<br>**#7** 'time'/exp<br>**#8** 'time*':ti,ab,kw<br>**#9** — #7 OR #8<br>**#10** — #3 AND #6 AND **#9** |

peroxide and carbamide peroxide, as our aim was to assess the effects of reduced application time on color change and tooth sensitivity, regardless of gel type. In addition, the limited number of clinical studies available and insufficient data for subgroup analyses by gel type and concentration required this combined approach. Random effects meta-analyses applying the inverse variance method were used to calculate effect measures and their corresponding 95% confidence intervals. Only studies classified as having a low and medium risk of bias of bias were included in the color change and tooth sensitivity analyses to evaluate the robustness of the findings.

Subgroup analyses for color change outcomes were performed to assess the effect of follow-up time on the reported results, with follow-up time as the main variable. The lack of sufficient data restricted the possibility of carrying out additional subgroup analyses by factors such as age group, type and concentration of bleaching agent. Additionally, was not possible to carry out a subgroup analysis for the tooth sensitivity results due to the lack of data reported during follow-up. Statistical heterogeneity was assessed using the $I^2$ index. Summary statistics and effect sizes from individual studies and summary effects from meta-analyses were reported in Forest Plots. Publication bias assessment, using funnel plots, was not considered due to the lack of power of the analyses as they included a small number of studies (less than 10) [21].

### Certainty of the evidence

The certainty of the estimates from the meta-analyses conducted was assessed using the Grading of Recommendations, Assessment, Development and Evaluation Pro software (GRADE pro-Guideline Development Tool, available online at gradepro.org). Risk of bias, inconsistency, indirectness, imprecision, and the possibility of publication bias were the contemplated aspects to rate the overall certainty of evidence [22].

## Results

### Study selection

A diagram describing the search and selection procedures, following the PRISMA guidelines [19] is illustrated in Fig. 1**.** The search was conducted until February 2024. After screening in databases and gray literature, and removing duplicates, a total of 6,011 studies were initially identified. Subsequently, 5,996 records were excluded based on eligibility criteria during the title and abstract screening phase. This led to the selection of 15 studies for comprehensive full-text assessment. After careful examination, 6 studies were excluded: four were protocols with previously published and retrieved articles, theses, or dissertations, while two did not have a comparator group. Nine studies were included for the data extraction and qualitative synthesis [1, 15, 17, 18, 23–27] and 8 for the quantitative synthesis [1, 15, 17, 18, 23, 24, 26, 27].

### Characteristics of included studies

Characteristics of the 9 selected studies are detailed in Table 2. The parallel study design was predominantly used in these studies [1, 15, 17, 18, 23, 25–27]. Only one study was performed under a split-mouth design [24]. The number of patients included in these studies ranged from 30 to 92 participants and the mean age ranged from 18.23 to 36.13. One study did not report this information [15].

Eight [1, 15, 17, 18, 23, 25, 27] out of the nine studies included in this systematic review evaluated both the objective ($\Delta E_{ab}$ and/or $\Delta E_{00}$) and the subjective (ΔSGU) color change. Only two [1, 24] evaluated the whitening index ($\Delta WI_D$). One reported only the $\Delta E_{ab}$ values [26]. Five studies used a shade guide Vita Classical and Vita Bleached [1, 15, 17, 24, 25] and two a shade guide Vitapan Classical [18, 27]. For objective color assessments, seven used the Vita Easyshade spectrophotometer [1, 15, 17, 18, 23, 24, 26] and two the Vivadent Easyshade spectrophotometer [25, 27].

For tooth sensitivity (TS) outcome all studies included [1, 15, 17, 18, 23–27] evaluated the intensity of TS and of these nine, six [1, 15, 17, 23, 25, 26] reported in their full texts both, the intensity and, also the risk of TS. Two employed the Visual Analogue Scale (VAS) [1, 23], two the Numeral Rating Scale (NRS) [24, 25], three the Verbal Evaluation Scale (VES) [18, 26, 27] and two used both, VAS and NRS to determine the intensity of TS [15, 17].

Variations were detected in the moments of assessment of color change and tooth sensitivity. Five articles exhibited the color outcomes measured 1-week [1, 15, 17, 23, 24], seven measured 2-weeks [15, 17, 18, 23–27] three measured 3-weeks [17, 23, 24], and one measured 4-weeks [17] during the bleaching procedures. In one study, the color outcomes were assessed after 16 days of the bleaching treatment [18]. In three articles, this outcome was evaluated after complete patient satisfaction, which was variable [18, 26, 27]. Six RCTs reported the follow-up of the patient's color assessment after the final bleaching procedures [1, 15, 17, 23, 24, 27]. Of these studies, two were evaluated after 2 weeks [23, 24], three after 1 month [15, 17, 27], and one after 6 and 12 months [1]. Regarding the evaluation of the TS, eight papers measured this outcome daily [15, 17, 18, 23–27], and one [1] measured 2, 7, and 14 days during the bleaching treatment. Three RCTs reported the follow-up for TS [1, 23, 24]. Of these

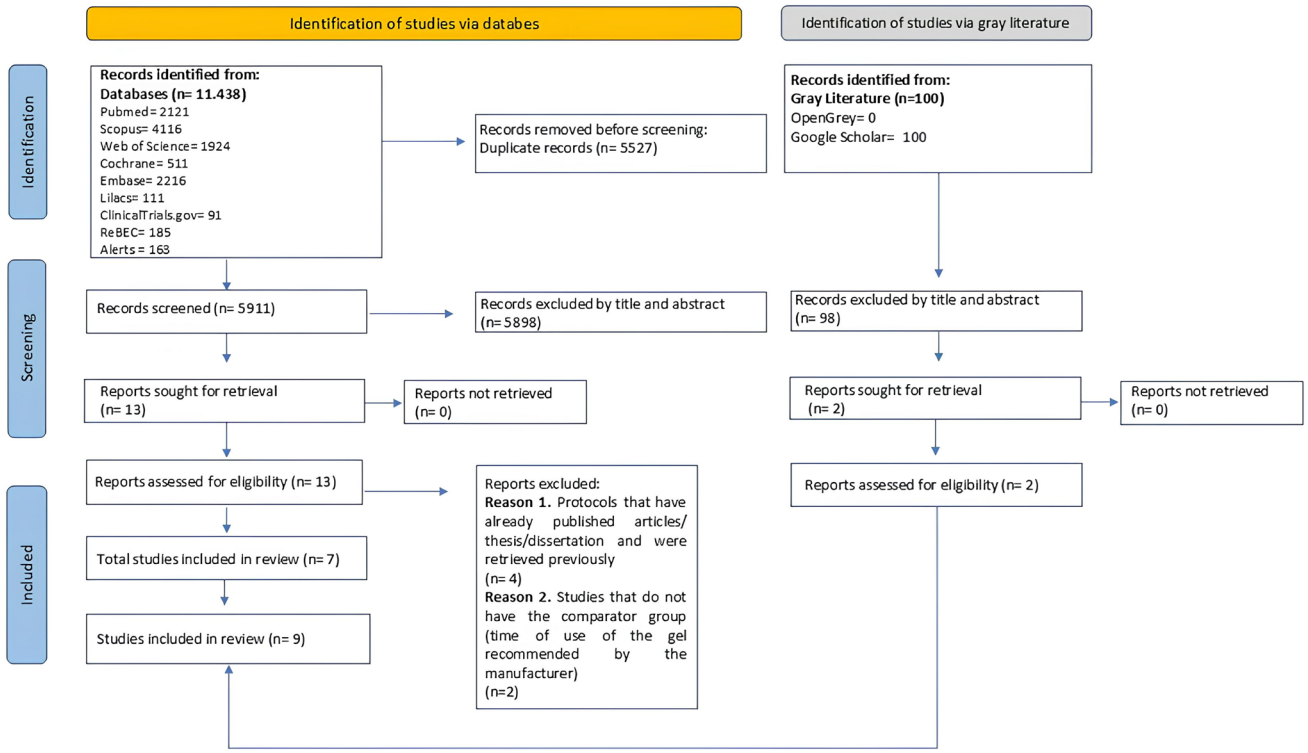


**Fig. 1** Flow diagram of literature searches

studies, two were evaluated after 2 weeks [23, 24] and one [1] after 48 h of the end treatment.

## Bleaching protocols

As shown in Table 2, most of the selected studies used CP 10% for at-home bleaching [1, 18, 23, 24, 26]. Four studies used HP varying from 4 to 10% [15, 17, 25, 27]. Variations in the bleaching protocol were observed mainly due to the presence of two types of bleaching agents (CP and HP), each characterized by varying concentrations and application times according to the manufacturer's specifications, as described in Table 2**.** However, in the studies that used CP 10%, the time indicated by the manufacturer was 8 h/daily, and the time of the treatment was variable. Two studies carried out the treatment during 21 days [23, 24], two during 14 days [1, 26] and one during 16 days [18]. More significant differences in bleaching protocols were observed in studies that used HP. The time indicated by the manufacturer was 60 min/daily in two studies [25, 27] and 30 and 120 min, respectively [15, 17]. The duration of treatment varied from 14 to 42 days.

## Assessment of risk of *bias*

The risk of bias in the eligible studies is presented in Fig. 2**.** The assessments were conducted for each outcome—color change analysis and tooth sensitivity—by RoB 2.0 guidelines. Since all studies included both color analysis (using either ΔE or ΔSGU) and sensitivity analysis (using either VAS or NRS), each outcome within a given study was assigned the same bias score, ensuring consistency in risk of bias assessment across the studies. Across both outcomes, all studies were classified as having either a low or moderate risk of bias in key domains. In the full-text evaluations, four studies [1, 15, 17, 26] were classified as low risk of bias according to the risk of bias used (RoB 2.0), as they met the five specific domains evaluated. Four studies were classified as having some concerns. Of these, three [18, 24, 27] don't report clearly the method of randomization employed and how the allocation concealment was performed in their full texts and one [23] about the measurement of the outcome, his domain was judged "unclear".

One study was considered a high risk of bias [25] because it started just a few months before the start COVID-19 pandemic and had to be stopped. Consequently, a substantial number of randomized patients were lost. In the full text of the manuscript, no consistent evidence indicates that the results reported were from all initially randomized patients. Therefore, it was not used in the meta-analysis.

## Results of syntheses

The effect measures considered to evaluate the influence of the time of use of the bleaching agent on color change and

**Table 2** Characteristics of the selected studies

| Study ID | Study design | Number of Patients | Sample age mean (SD) [range] | Groups | | Outcome assessment method | | | Assessment periods |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Intervention details | Comparison details | Color change | Tooth Sensitivity | Patient Satisfaction | |
| Pavani et al., 2023 (Brazil) | Parallel | 66 | n.r ± n.r [18-21] | Bleaching agent: CP<br>Concentration: 10%<br>Times:<br>2 h daily **(n = 22)**<br>4 h daily **(n = 22)**<br>21 days of treatment | Bleaching agent: CP<br>Concentration: 10%<br>Time:<br>8 h daily **(n = 22)**<br>21 days of treatment | ΔSGU (Vita Classical), $\Delta E_{00}$ (Spectrophotometer, Vita Easyshade) and $\Delta E_{ab}$* (Spectrophotometer, Vita Easyshade) | VAS | Self-report questionnaire | **Color Change:** Baseline After 1 week<br>After 2 weeks<br>After 3 weeks<br>2 weeks after the final treatments **Tooth Sensitivity:** Daily<br>2 weeks after the final treatments |
| Pavani 2022 (Brazil) | Split-mouth | 58 | n.r. ± n.r. [18–30] | Bleaching agent: CP<br>Concentration: 10%<br>Times:<br>GI – 1 h daily **(n = 20)**<br>GII – 2 h daily **(n = 20)**<br>GIII – 4 h daily **(n = 18)** 21 days of treatment | Bleaching agent: CP<br>Concentration: 10%<br>Times:<br>GI – 8 h daily **(n = 20)**<br>GII – 8 h daily **(n = 20)**<br>GIII – 8 h daily **(n = 18)** 21 days of treatment | ΔSGU (Vita Classical and Vita Bleachedguide 3D-MASTER), ΔE00 and $\Delta WI_D$ (Spectrophotometer, Vita Easyshade) | NRS | VAS | **Color Change:** Baseline After 1 week<br>After 2 weeks<br>After 3 weeks<br>2 weeks after the final of treatments **Tooth Sensitivity:** Daily 2 weeks after the final of treatments |
| Terra et al., 2021 (Brazil) | Parallel | 92 | n.r. ± n.r. [18–42] | Bleaching agent: HP<br>Concentration: 4%<br>Time: 30 min daily **(n = 46)** 28 days of treatment | Bleaching agent: HP<br>Concentration: 4%<br>Time: 120 min daily **(n = 46)** 28 days of treatment | ΔSGU (Vita Classical and Vita Bleachedguide 3D-MASTER), $\Delta E_{ab}$ and $\Delta E_{00}$ (Spectrophotometer, Vita Easyshade) | NRS and VAS | Likert scale | **Color Change:** Baseline After 1 week After 2 weeks After 3 weeks After 4 weeks* After 1 month **Tooth Sensitivity:** Daily |
| Chemin et al., 2021 (Brazil) | Parallel | 72 | n.r. ± n.r. [n.r.] | Bleaching agent: HP<br>Concentration: 10%<br>Time: 15 min daily **(n = 36)**<br>14 days of treatment | Bleaching agent: HP<br>Concentration: 10%<br>Time: 30 min daily **(n = 36)** 14 days of treatment | ΔSGU (Vita Classical and Vita Bleachedguide 3D-MASTER) and ΔEab (Spectrophotometer, Vita Easyshade) | NRS and VAS | n.r | **Color Change:** Baseline After 1 week After 2 weeks After 1-month **Tooth Sensitivity:** Daily |

**Table 2** (continued)

| Study ID | Study design | Number of Patients | Sample age mean (SD) [range] | Groups | | Outcome assessment method | | | Assessment periods |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Intervention details | Comparison details | Color change | Tooth Sensitivity | Patient Satisfaction | |
| Mota 2021 (Brazil) | Parallel | 63 | n.r. ± n.r. [18–40] | Bleaching agent: HP Concentration: 6% Times: 15 min daily **(n = 21)** 30 min daily **(n = 22)** Approximately 28 days of treatment | Bleaching agent: HP Concentration: 6% Time: 60 min daily **(n = 20)** Approximately 28 days of treatment | ΔSGU (Vita Classical and Vita Bleached guide 3D-MASTER) and ΔE (Spectrophotometer, Easyshade—Vivadent) | NRS | Self-report questionnaire and PIDAQ | **Color Change:** Baseline After 2 weeks Final treatment (variable) **Tooth Sensitivity:** Daily |
| Mailart et al., 2021 (Brazil) | Parallel | 30 | 21.08 ± 2.06 [n.r.] | Bleaching agent: CP Concentration: 10% Time: 2 h daily **(n = 15)** 14 days of treatment | Bleaching agent: CP Concentration: 10% Time: 8 h daily **(n = 15)** 14 days of treatment | ΔSGU (Vita Classical and Vita Bleachedguide 3D-MASTER), $\Delta E_{ab}$, $\Delta E_{00}$ and $\Delta WI_D$ (Spectrophotometer, Vita Easyshade) | VAS | Self-report questionnaire | **Color change:** Baseline 2 weeks 3 weeks 6 months 12 months **Tooth Sensitivity:** 2, 7 and 14 days after the treatment; 48 h after the end of treatments |
| Darriba et al., 2017 (Brazil) ¥ | Parallel | 40 | 30.09 ± 10.19 [n.r.] | Bleaching agent: (a) CP Concentration: 10% Time: 1 h daily **(n = 20)**; (b) HP Concentration: 7,5% Time: 1 h daily **(n = 20)**;14 days of treatment | Bleaching agent: CP Concentration: 10% Time: 8 h daily **(n = 20)** 14 days of treatment | $\Delta E_{ab}$ (Spectrophotometer, Vita Easyshade) | VES | n.r | **Color Change:** Baseline 2 weeks After the final treatment (variable) **Tooth sensitivity:** Daily |
| Carneiro 2016 (Brazil) | Parallel | 60 | n.r. ± n.r. [18–60] | Bleaching agent: HP Concentration: 7,5% Times: 10 min daily **(n = 20)** 30 min daily **(n = 20)** 14—42 days of treatment | Bleaching agent: HP Concentration: 7,5% Time: 60 min daily **(n = 20)** 14—42 days of treatment | ΔSGU (Vitapan Classical Shade Guide and $\Delta E_{ab}$ (Easyshade Advance 4.0, Vident, Brea) | VES | Self-report questionnaire | **Color Change:** Baseline After 2 weeks After the final treatment (variable) 1 month after bleaching **Tooth Sensitivity:** Daily |

**Table 2** (continued)

| Study ID | Study design | Number of Patients | Sample age mean (SD) [range] | Groups | | Outcome assessment method | | | Assessment periods |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Intervention details | Comparison details | Color change | Tooth Sensitivity | Patient Satisfaction | |
| Cardoso et al., 2010 (Brazil) | Parallel | 60 | n.r. ± n.r. [17–30] | Bleaching agent: CP<br>Concentration: 10%<br>Times:<br>15 min daily **(n = 15)**<br>30 min daily **(n = 15)** 1 h daily **(n = 15)** 16 days of treatment | Bleaching agent: CP<br>Concentration: 10%<br>Time:<br>8 h daily **(n = 15)**<br>16 days of treatment | ΔSGU (Vitapan Classical Shade Guide and $\Delta E_{ab}$ (Spectrophotometer, Vita Easyshade) | VES | Self-report questionnaire | **Color Change:**<br>Baseline After the 16-day bleaching protocol<br>After the final treatment (variable)<br>After complete satisfaction patient achieved<br>**Tooth sensitivity:**<br>Daily |

ID–identification CP-carbamide peroxide; HP-hydrogen peroxide; n.r-not reported; TS-tooth sensitivity; VAS-visual analogical scale; $\Delta E_{ab}$ and $\Delta E_{00}$-objective color change; ΔSGU-subjective color change; $\Delta WI_D$-Whitening index; NRS-numerical rating scale; VES-Verbal Evaluation Scale; PIDAQ-Psychosocial Impact of Dental Aesthetics Questionnaire

(*): Data extracted from a file recovered before publication of the article in the Scientific Journal

(¥): The study entered the meta-analysis twice, once in each subgroup: (a) CP 10% and (b): HP 7.5%

tooth sensitivity were the mean difference (MD) for continuous outcomes ($\Delta E_{ab}$, $\Delta E_{00}$, $WI_D$, ΔSGU—classical, ΔSGU—Bleached) and the Relative Risk (RR) for dichotomous outcomes (Tooth sensitivity). Subgroup analyses were performed to assess the effect of follow-up time on the reported results for color change. A meta-analysis on the intensity of TS was not performed due to significant variations in the data reported in different studies. Despite efforts to gather additional information by contacting the authors via email, compiling a meta-analysis focusing specifically on the intensity of TS was not feasible. Measures were taken to reduce the discrepancy in the moments of assessment of color change outcome. We conducted a meta-analysis based on two specific evaluation points: two weeks after the bleaching procedure and during a short-term follow-up period, defined as three weeks or more after the treatment's completion. The duration of this follow-up varied depending on the specific bleaching protocol employed. In the following results of the meta-analysis, values in parentheses represent the 95% confidence intervals (CIs) for each measure.

## Color Change—$\Delta E_{ab}$

It was observed that the use of at-home bleaching gel for the time indicated by the manufacturer promoted higher $\Delta E_{ab}$ with a statistical difference for two weeks and, also at short short-term follow-up ($p < 0.0001$ and $p = 0.04$, respectively). The MD at two weeks was -1.69 (-2.44, -0.93) and -0.96 (-1.85, -0.06) for the short-term follow-up. **(**Fig. 3**).**

## Color Change—$\Delta E_{00}$

As shown in Fig. 4, there was no difference between the studies after two weeks ($p = 0.13$) with the MD. However, when we look at short-term follow-up there's a significant difference that favors using the gel within the time indicated by the manufacturer ($p < 0.0001$). The overall MD was -1.13 (-1.60, -0.67)**.**

## Color Change—$WI_D$

Similarly, the group that used the bleaching gel for the period recommended by the manufacturer showed better $WI_D$ results than those that bleached for a shorter period. ($p = 0.002$ – two weeks; $p = 0.0010$ – short-term follow-up). The overall MD was -2.93 (-4.79, -1.08) and -2.78 (-4.44, -1.13), respectively **(**Fig. 5**).**

## Subjective Color Change ΔSGU—Classical

The included studies demonstrated that the reduced time of use of at-home bleaching gel compared to use for the

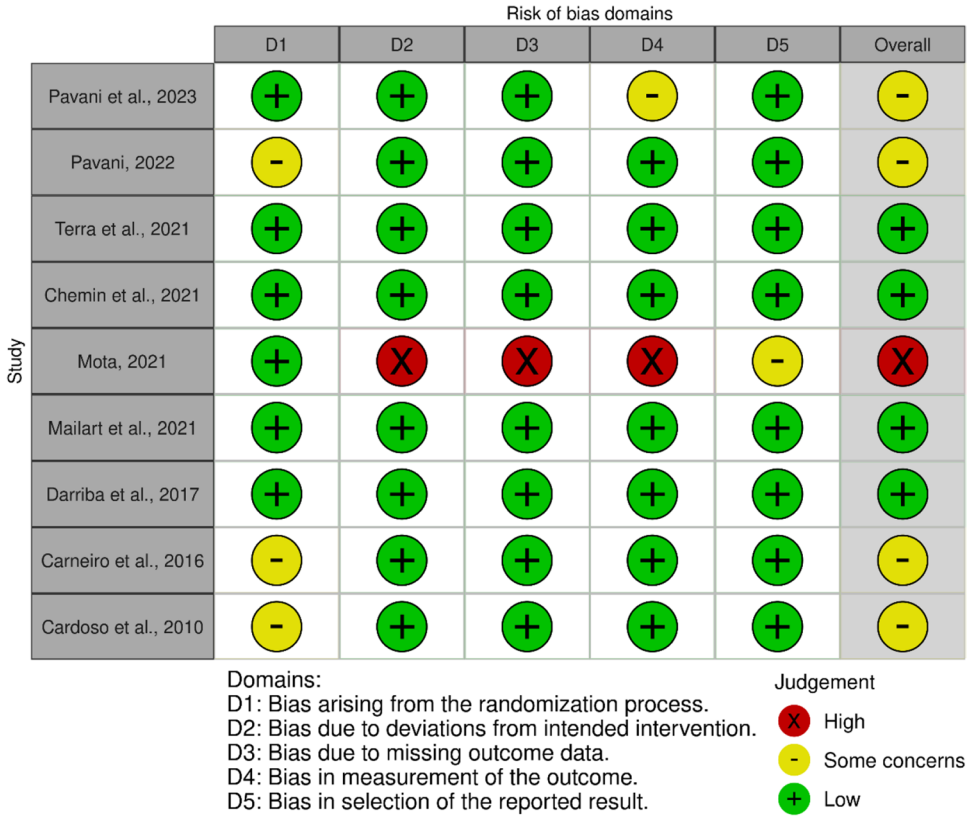


**Fig. 2** Summary of risk of bias assessment for all outcomes (color change and tooth sensitivity)

time indicated by the manufacturer influenced subjective color change ΔSGU—Classical outcome. Significant differences were detected at two weeks (p = 0.0008) and short-term follow-up (p = 0.0004) after bleaching favoring the use of the gel within the time indicated by the manufacturer. The overall MD was -0.98 (-1.55, -0.40) and -0.96 (-1.50, -0.43). The data from the evaluated subgroups were considered homogeneous (p = 0.21, $I^2$ = 36%; p = 0.22, $I^2$ = 31%) (Fig. 6).

### Subjective Color Change ΔSGU—Bleached

ΔSGU—Bleached shows that no differences were detected at two weeks (p = 0.09) and short-term follow-up (p = 0.18) after bleaching when compared to the reduced use time of at-home bleaching gel and the time indicated by the manufacturer. The overall MD was -0.55 (- 1.19, 0.08) and -0.52 (-1.28, 0.24). The data from the evaluated subgroups did not present heterogeneity (p = 0.27, $I^2$ = 23%; p = 0.17, $I^2$ = 44%) (Fig. 7).

### Relative Risk of TS

The use of a reduced time of at-home bleaching gel favored a reduction in the incidence of tooth sensitivity events, as a statistical difference was found between the intervention and comparison groups (p = 0.03). The overall RR was 0.80 (0.66, 0.98). We did not detect heterogeneity in the data (p = 0.30, $I^2$ = 17%) (Fig. 8).

## Assessment of the certainty of evidence

Table 3 presents an overview of the GRADE assessment detailing the certainty of evidence for the RCTs. The certainty of the evidence ranged from very low to moderate. The items most affected were the imprecision and risk of bias of the studies evaluated. The imprecision for the continuous outcomes ($\Delta E_{ab}$, $\Delta E_{00}$, $\Delta WI_D$, ΔSGU-Classical and ΔSGU-Bleached) was considered to be affected by a limited number of individuals included in the analyses (the GRADE rule of thumb indicates a minimum number of 400 for continuous outcomes) and by the confidence interval which included 0 (lack of effect) and additionally included values which demonstrate a clinically important effect in one of the directions (interval limit greater than 1 unit). In addition, for dichotomous outcomes (TS) the imprecision of the studies was also affected by a limited number of individuals included in the analyses (the GRADE rule of thumb indicates a minimum number of 2,000 or perhaps 4,000 for dichotomous outcomes), and also by the confidence interval that included 1 (lack of effect) and additionally included values that demonstrate a clinically important effect in one of the directions (the lower limit shows a RR reduction greater than 25%).

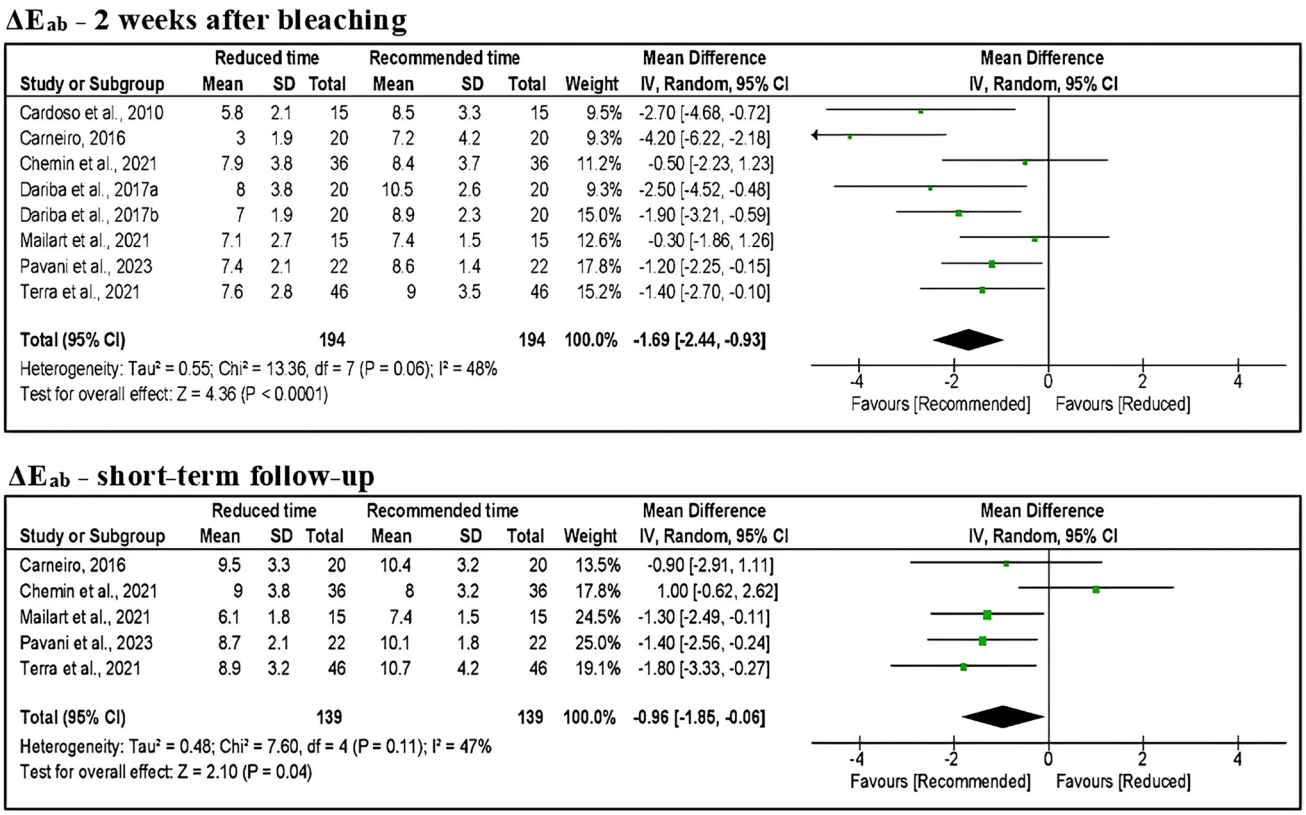


**Fig. 3** Forest plot of objective color change ($\Delta E_{ab}$) obtained with protocols using the at-home bleaching gel for the time indicated by the manufacturer and in a reduced time

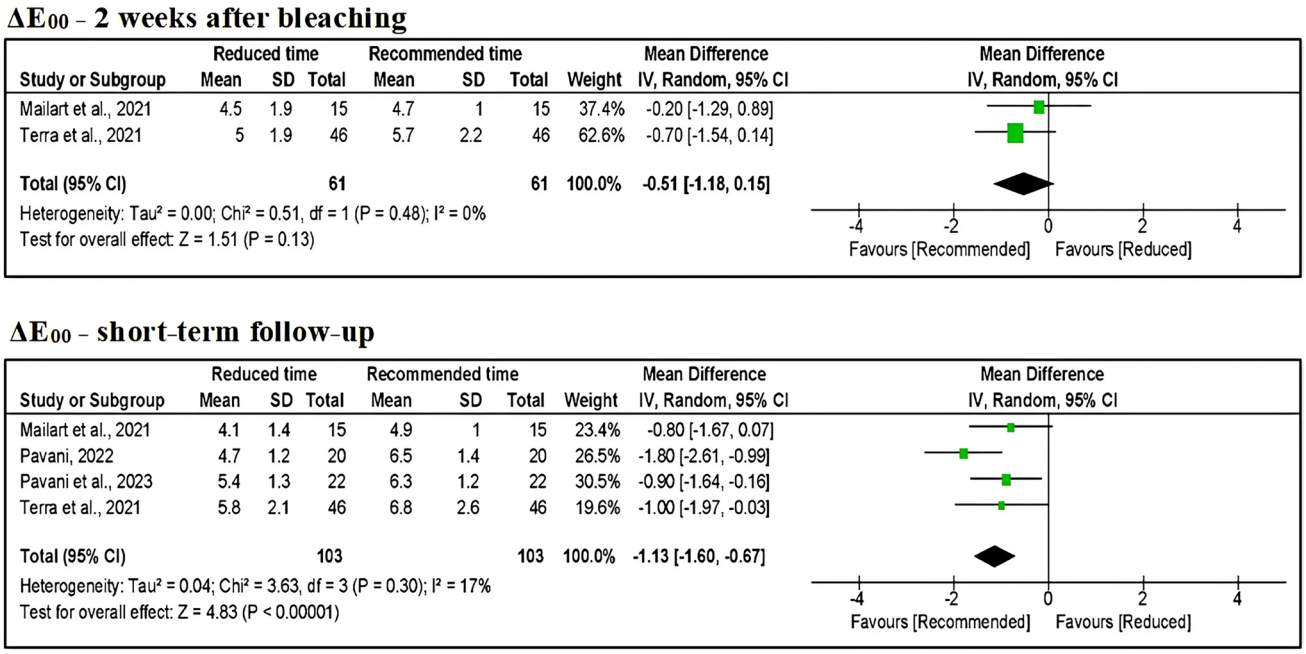


**Fig. 4** Forest plot of objective color change ($\Delta E_{00}$) obtained with protocols using the at-home bleaching gel for the time indicated by the manufacturer and in a reduced time

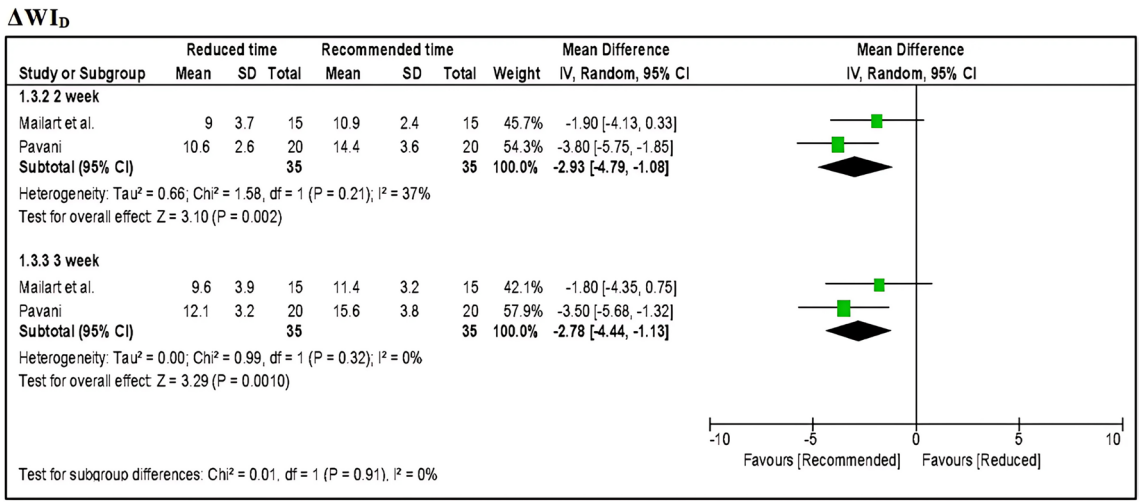


**Fig. 5** Forest plot of objective color change **($WI_D$)** obtained with protocols using the at-home bleaching gel for the time indicated by the manufacturer and in a reduced time

On the other hand, the risk of bias was considerably affected by data from some studies with methodological limitations that could have compromised the validity of the estimates.

## Discussion

When performing at-home bleaching, the professional must choose the type and concentration of bleaching gel for each patient. Each manufacturer indicates a specific time for using the tray with the gel. This systematic literature review compared whether reducing this manufacturer-indicated time maintains the bleaching effect while reducing tooth sensitivity. However, due to methodological differences, the certainty of the evidence was classified from low to moderate. Although RCTs generally exhibit high initial quality, it is important to note that limitations in study design, uncertainty about the direction of results, and significant data inconsistency can negatively impact the level of evidence. To ensure consistency in the certainty of evidence,

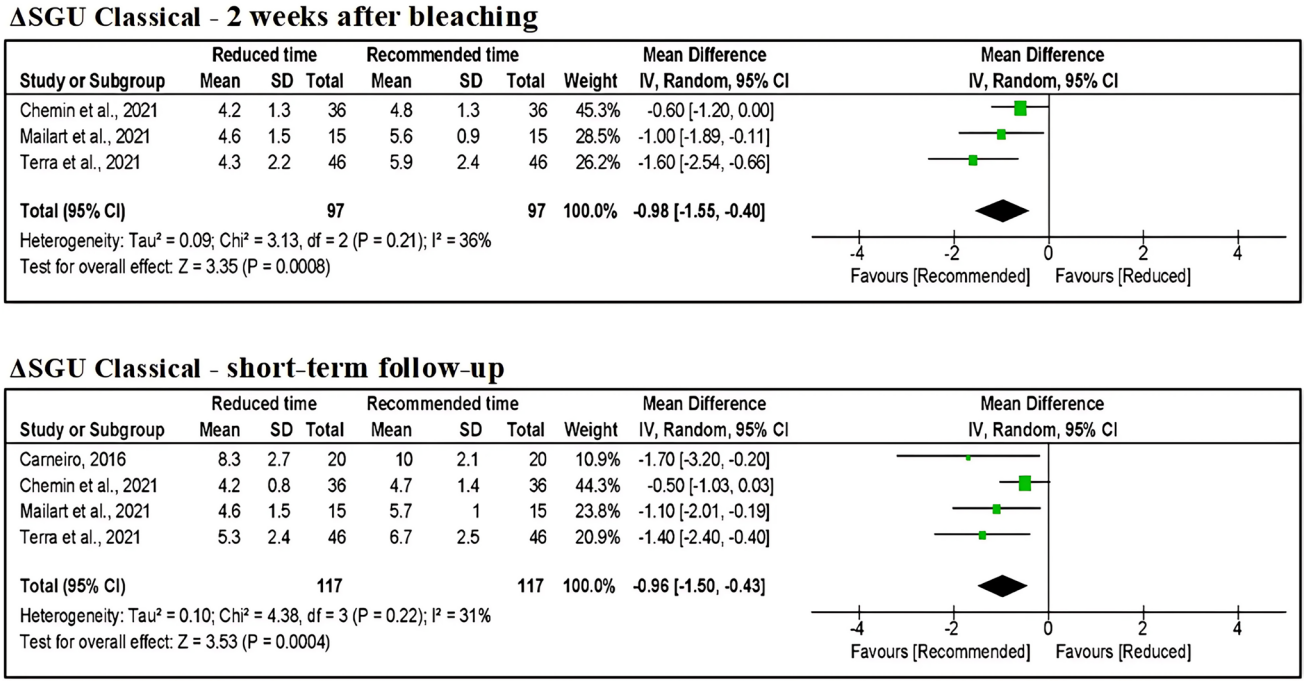


**Fig. 6** Forest plot of subjective color change **(ΔSGU – Classical)** obtained with protocols using the at-home bleaching gel for the time indicated by the manufacturer and in a reduced time

a global analysis of the results was conducted, including studies with some concerns regarding risk of bias, as long as their impact on evidence certainty was not significant. Both bias and imprecision, however, affected the overall quality of the evidence, as discussed above. The risk of bias assessments for each outcome—color change analysis and tooth sensitivity—were conducted in accordance with RoB 2.0 guidelines, providing a structured evaluation across key domains. Therefore, although these studies were included in the analysis, their presence may affect confidence in the results, highlighting the need for caution when interpreting the conclusions.

The present study demonstrated that the use of bleaching gel for the time recommended by the manufacturer resulted in better whitening efficacy than that observed when the application time shortened, as observed in both the objective assessment ($\Delta E_{ab}$) and the subjective assessment (ΔSGU-Classical) of color. These differences were noted in both the evaluation after two weeks of treatment and the short-term assessment, with the certainty of the

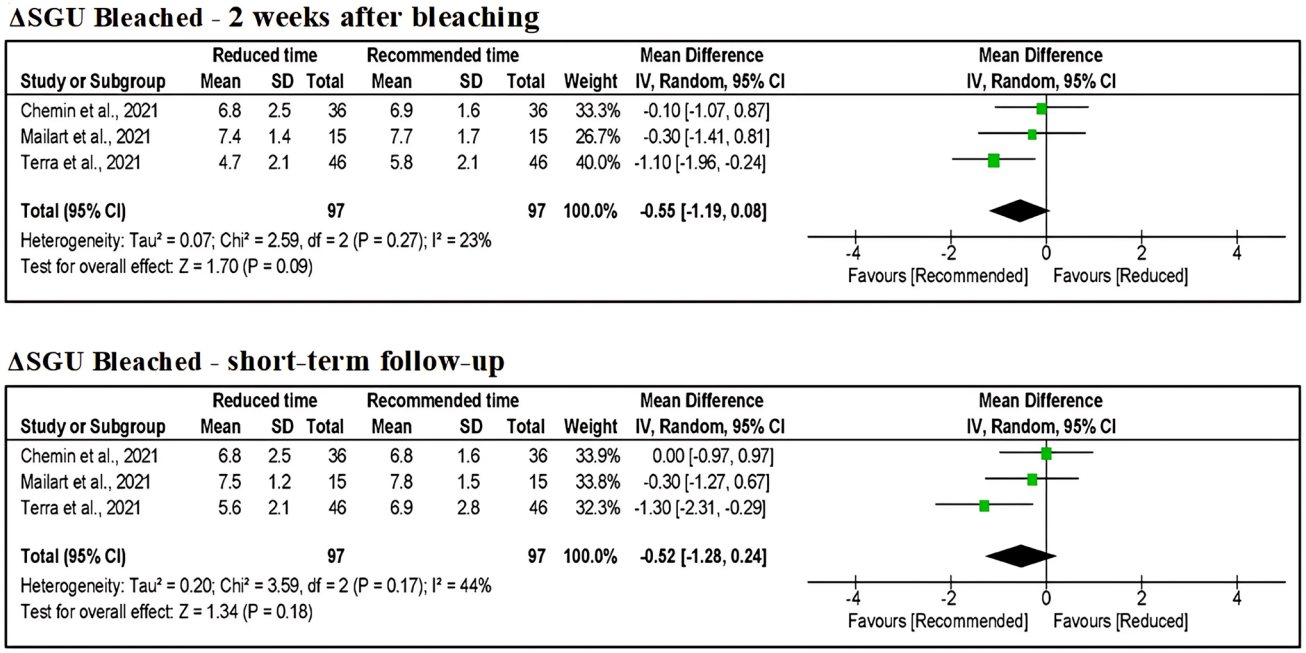


**Fig. 7** Forest plot of subjective color change **(ΔSGU – Bleached)** obtained with protocols using the at-home bleaching gel for the time indicated by the manufacturer and in a reduced time

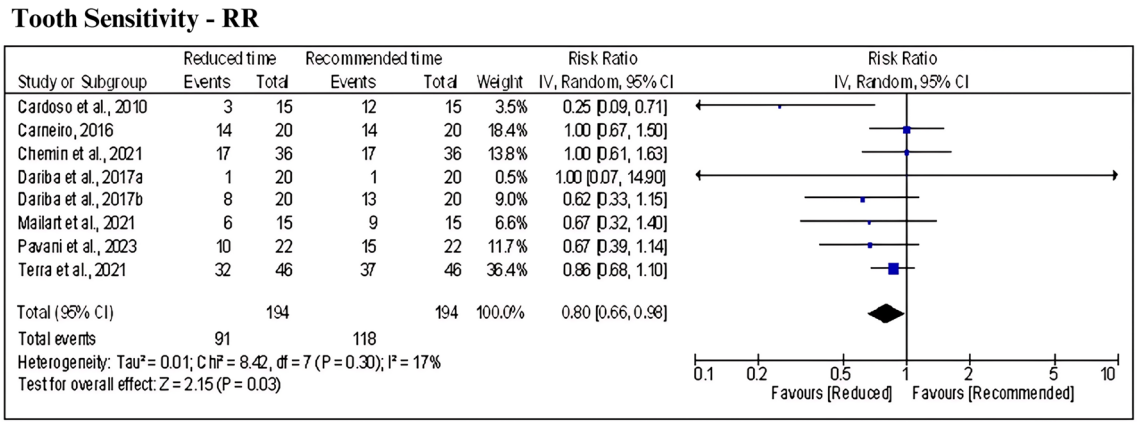


**Fig. 8** Forest plot of **relative risk of TS** obtained with protocols using the at-home bleaching gel for the time indicated by the manufacturer and in a reduced time

**Table 3** Summary of the findings and the quality of evidence assessment according to GRADE

| Certainty assessment | | | | | | | # of participants | Absolute effect | Overall certainty |
|---|---|---|---|---|---|---|---|---|---|
| # of studies | Design of the studies | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | | MD (95% CI)* OR (95% CI)** | |
| $\Delta E_{ab}$ (2 weeks after bleaching) | | | | | | | | | |
| 8 | Randomized clinical trials | Not serious● | Not serious | Not serious | Serious[a] | None | 388 | MD: -1.69 (-2.44, -0.93) | ⨁⨁⨁◯ MODERATE |
| $\Delta E_{ab}$ (short-term follow-up) | | | | | | | | | |
| 5 | Randomized clinical trials | Serious | Not serious | Not serious | Serious[a] | None | 278 | MD: -0.96 (-1.85, -0.06) | ⨁⨁◯◯ LOW |
| $\Delta E_{00}$ (2 weeks after bleaching) | | | | | | | | | |
| 2 | Randomized clinical trials | Not serious | Not serious | Not serious | Very Serious[a,,b] | None | 122 | MD: -0.51 (-1.18, 0.15) | ⨁⨁◯◯ LOW |
| $\Delta E_{00}$ (short-term follow-up) | | | | | | | | | |
| 4 | Randomized clinical trials | Not serious● | Not serious | Not serious | Serious[a] | None | 206 | MD: -1.13 (-1.60, -0.67) | ⨁⨁⨁◯ MODERATE |
| ΔSGU-Classical (2 weeks after bleaching) | | | | | | | | | |
| 3 | Randomized clinical trials | Not Serious | Not serious | Not serious | Serious[a] | None | 194 | MD: -0.98 (-1.55, -0.40) | ⨁⨁⨁◯ MODERATE |
| ΔSGU-Classical (short-term follow-up) | | | | | | | | | |
| 4 | Randomized clinical trials | Not serious | Not serious | Not serious | Serious[a] | None | 234 | MD: -0.96 (-1.50, -0.43) | ⨁⨁⨁◯ MODERATE |
| ΔSGU-Bleached (2 weeks after bleaching) | | | | | | | | | |
| 3 | Randomized clinical trials | Not serious | Not serious | Not serious | Very serious[a,b] | None | 194 | MD: -0.55 (-1.19, 0.08) | ⨁⨁◯◯ LOW |
| ΔSGU-Bleached (short-term follow-up) | | | | | | | | | |
| 3 | Randomized clinical trials | Not serious | Not serious | Not serious | Very serious[a,b] | None | 194 | MD: -0.52 (-1.28, 0.24) | ⨁⨁◯◯ LOW |
| $\Delta WI_D$ (2 weeks after bleaching) | | | | | | | | | |
| 2 | Randomized clinical trials | Not serious● | Not serious | Not serious | Serious[a] | None | 70 | MD: -2.93 (-4.79, -1.08) | ⨁⨁⨁◯ MODERATE |
| $\Delta WI_D$ (short-term follow-up) | | | | | | | | | |
| 2 | Randomized clinical trials | Not serious● | Not serious | Not serious | Serious[a] | None | 70 | MD: -2.78 (-4.44, -1.13) | ⨁⨁⨁◯ MODERATE |
| Tooth Sensitivity | | | | | | | | | |
| 6 | Randomized clinical trials | Serious[c] | Not serious | Not serious | Very serious[d,e] | None | 314 | RR: 0.80 (0.66, 0.98) | ⨁⨁⨁◯ VERY LOW |

* For continuous outcomes

** For dichotomous outcomes

● The exclusion of data from studies with "some concerns" related to risk of bias did not alter the direction and/or significance of the estimates. Therefore, data were maintained to gain precision

a Limited number of subjects included in the analyses (GRADE rule of thumb indicates a minimum number of 400 for continuous outcomes)

b Confidence interval includes 0 (lack of effect), and additionally includes values that demonstrate a clinically important effect in one of the directions (interval limit greater than 1 unit)

c Data from some studies with methodological limitations that could have compromised the validity of the estimates

d Limited number of subjects included in the analyses (GRADE rule of thumb indicates a minimum number of 2000 or perhaps 4000 for dichotomous outcomes)

e Confidence interval includes 1 (lack of effect), and additionally includes values that demonstrate a clinically important effect in one of the directions (lower limit shows relative risk reduction greater than 25%)

evidence considered to be low to moderate. These two different time points were adopted in the meta-analyses based on the different evaluation times reported by the included studies. Randomized clinical trials on tooth bleaching normally point out the color outcomes not only immediately after the last bleaching session, but also a few weeks later so that color stabilization would demonstrate the final esthetic outcome [28–31].

Objective color analysis in dentistry relies primarily on ΔE standards based on CIEL*a*b* and CIEDE 2000 coordinates, gathered through spectrophotometers [32]. The CIEL*a*b* system, which considers *L (lightness), *a (green–red), and *b (blue-yellow) coordinates, has been widely utilized for color characterization in Dentistry. However, CIEDE 2000 was developed to correct hue and chroma interactions, in the *b coordinate and the low influence of the *a coordinate on tooth structure, which is important only for colors with low chroma [33, 34]. The objective analysis using CIEDE 2000 ($\Delta E_{00}$) demonstrated no significant difference between the groups regarding color change immediately after a two-week bleaching regimen. However, the manufacturer's recommended time promoted significantly higher $\Delta E_{00}$ in the short-term assessment. Differences between these two time points could be a result of only two studies being included in the evaluation immediately after a 2-week home bleaching. Currently, CIEDE 2000 stands as the most advanced and recommended formula by CIE for clinical instrumental analyses as it aligns better with visual perception [35, 36]. However, most studies included in this systematic review employed the CIEL*a*b* system, resulting in few studies reporting the CIEDE 2000 [33, 34].

Meanwhile, subjective evaluation using ΔSGU-Bleached did not show significant differences in color change for both the two weeks of treatment and short-term follow-up [1, 15, 17]. The certainty of the evidence from these analyses ranged from low to moderate. Although objective analyses offer a potential advantage compared to subjective analysis, it is important to emphasize that subjective color analysis (ΔSGU) is a widely employed method, based on the use of a commercial shade guide to clinically assess tooth coloration. However, it is considered a subjective method, as ocular fatigue, age, and lighting conditions can directly influence tooth color determination [37]. For this purpose, there are several color scales available. However, studies indicate that the VITA Bleachguide (ΔSGU-Bleached) may provide a more consistent visual assessment of whitening efficacy compared to the VITA Classical scale (ΔSGU-Classical), due to its wider range of colors and more uniform distribution. Additionally, the Bleachguide scale shows a higher correlation between visual grading and instrumental results (Easyshade), enabling a more precise, consistent, and reliable evaluation of bleaching treatment [38].

The studies by Pavani et al., (2022) [24], Cardoso et al., (2010) [18], and Carneiro et al., (2016) [27], presented heterogeneity regarding the randomization for the objective analyses CIEDE 2000 ($\Delta E_{00}$) and subjective ΔSGU-Classical and ΔSGU-Bleached, while Pavani et al., (2023) [23], presented heterogeneity regarding the measurement of the results classifying them as some concern risk of bias. Nonetheless, despite the high heterogeneity observed in the number of participants across the studies, considerable consistency is observed concerning the presented results, as suggested by the GRADE analysis. Consequently, despite the inclusion of these studies, their discrepancies did not substantially impact the meta-analysis outcome, as they did not introduce significant alterations to the overall result. Thus, despite the inclusion of these studies, the meta-analysis was not affected, as the results were not changed.

The Whitening Index for Dentistry ($WI_D$) has recently begun to evaluate bleaching perceptibility and relate visual assessments to CIEL*a*b* coordinates [33]. Thus, applying this index reduces the subjectivity of visual analysis and quantifies the bleaching effect. High positive values of $WI_D$ indicate greater perceptibility of bleaching, while low values are related to lower perceptibility of bleaching [33, 39]. Only two studies [1, 24] conducted the $\Delta WI_D$ analysis. The results of $\Delta WI_D$, at the 2-week evaluation and short-term follow-up, showed significant differences for the group that used the manufacturer's recommended bleaching gel application time.

The study of Pavani et al., (2022) [24] did not alter the direction or significance of the estimates. However, the certainty of the evidence is low. The recent introduction of $\Delta E_{00}$ and $\Delta WI_D$ scales in RCTs has limited the inclusion of studies, underscoring the imperative for future research endeavors that contribute to advancing knowledge in this area. Expectations that reduced gel usage time during at-home bleaching would advance bleaching efficacy were not universally observed, likely due to protocol variations and bleaching product concentrations. Future studies evaluating $\Delta E_{00}$ and $\Delta WI_D$ further contribute to the challenge of establishing this association.

There are discrepancies among the studies when analyzing the results regarding color change. This disparity can be attributed to the various protocols employed, which involve different types of peroxides (HP and CP), variations in the concentrations of these peroxides, and different application times. However, it is important to highlight some specific results that deserve attention. Studies that used HP-based gels observed faster bleaching effects than those using CP [15, 27]. This occurs because CP-based gels need to first decompose into HP and urea after exposure to moisture conditions before achieving the bleaching effect [15]. However, the same did not happen in the study by Terra et al., (2021)[17].

Overall, the certainty of evidence was assessed as low to moderate for the color outcome in both analyzed periods (after two weeks of treatment and short-term follow-up). The factors contributing to this assessment were imprecision due to the limited number of participants included in the analyses (< 400) and the inclusion of studies with some concerns about the risk of bias. However, it is important to emphasize that despite the inclusion of these studies in the meta-analysis, neither the direction nor the significance of the estimates was influenced, thus justifying their retention to ensure greater precision of the results [40].

Regarding tooth sensitivity, relative risk data were used, which showed low heterogeneity ($I^2 = 17\%$), and all studies were included in the meta-analysis. The results revealed that reducing the gel application time during at-home bleaching demonstrated a statistically significant difference, suggesting a decrease in sensitivity. However, despite this, the certainty of the evidence was considered very low, and the confidence interval includes the possibility of no effect. Due to limitations and heterogeneity in the authors' reports concerning the sensitivity analysis, it is important to note that a meta-analysis on the intensity of tooth sensitivity could not be conducted. The authors were contacted by email and were unable to provide adequate data to be included in the analysis.The tooth bleaching mechanism, known as the "chromophore theory," primarily involves hydrogen peroxide interacting with organic chromophores within the tooth structure. However, peroxide diffusion into dental tissues is influenced by specific chemical affinities for each tissue. As HP diffuses into the tooth, it interacts with both chromophores and healthy structures [41]. That way, post-bleaching sensitivity may be at least in part a consequence of the diffusion of HP through the enamel and dentin into the pulp chamber [42]. This phenomenon results in pulp inflammation, with the release of inflammatory mediators and sensory nerve stimuli. Thus, controlling concentration and application time is crucial to minimize peroxide penetration into the pulp cavity while maintaining bleaching efficacy [41, 42].

Consequently, higher concentrations of bleaching gels do not ensure superior outcomes [43]. The increase in gel concentration and contact time with the tooth surface can result in greater diffusion of HP into the pulp chamber. This situation was reported by Cardoso et al., (2010) [18], which demonstrated that the longer the contact time of the gel with the tooth surface, the higher the risk of sensitivity. Thus, it is essential to control these factors to prevent potential damage to pulp cells in both at-home and in-office bleaching techniques[42–44].

It is important to emphasize that, in addition to the gel concentration and contact time with the tooth surface, the composition and pH of the products can influence the penetration of HP into the pulp chamber, such as the presence of restorations, cracks, tooth thickness/type, and cervical lesions. All these factors may account for the variability in results for tooth sensitivity [45].

Color and tooth sensitivity analyses are important parameters for the professional to measure whether the treatment is effective without causing any adverse effects to the patient. However, patient satisfaction level is also important for them to gauge whether the treatment has met their expectations. Although the studies conducted satisfaction analysis, the heterogeneity of the analyses performed did not allow for a meta-analysis. However, it can be observed from the results of each study that reducing the usage time of the individual tray did not influence patient satisfaction with the treatment.

The few studies found in the literature search and included in the meta-analysis prevented the evaluation of some variables, such as different protocols and product concentrations, in the results through a meta-analysis. Thus, despite presenting homogeneity, the certainty of the evidence was considered low and moderate, suggesting limited confidence and an estimated effect. Therefore, more randomized clinical trials (RCTs) using the same protocol and equivalent gel concentrations should be conducted. Additionally, RCTs must adopt an adequate randomization process, allocation concealment, and sample size determination.

## Conclusion

The evidence suggests that reducing exposure time to at-home bleaching gel reduces tooth sensitivity events; however, most of the parameters that assess color change favor using at-home bleaching gel for the time recommended by the manufacturer. However, the current evidence has methodological limitations and needs to be more precise (low to moderate) to reach definitive conclusions. Therefore, further studies are required.

**Author Contribution** • P. B. G. M.: Writting - original draft, Methodology, Formal analysis. • L. V. S. S.: Writing – original draft, Methodology, Formal analysis. • L. C. M.: Writing – review & editing, Supervision, Project administration. • G. A. M. V.: Writing – review, editing, Data curation. • M. K.: Writing – review & editing. • V. C.: Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. All authors reviewed the manuscript.

**Funding** This study was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) – Process number: 2021/14834–7. Coordenação de Aperfeiçoamento de Pessoal de Nível Superior–Brasil (CAPES), Grant/Award Number: Finance Code 001.

## Declarations

**Ethics approval and consent to participate** Not Applicable.

**Conflict of interests** The authors declare no competing interests.

## References


1. Mailart MC, Sakassegawa PA, Santos KC, Torres CRG, Palo RM, Borges AB (2021) One-year follow-up comparing at-home bleaching systems outcomes and the impact on patient's satisfaction: Randomized clinical trial. J Esthet Restor Dent 33:1175–1185. https://doi.org/10.1111/jerd.12814
2. Kothari S, Gray AR, Lyons K, Tan XW, Brunton PA (2019) Vital bleaching and oral-health-related quality of life in adults: A systematic review and meta-analysis. J Dent 84:22–29. https://doi.org/10.1016/j.jdent.2019.03.007
3. Joiner A (2006) The bleaching of teeth: a review of the literature. J Dent 34:412–419. https://doi.org/10.1016/j.jdent.2006.02.002
4. Goettems ML, Fernandez MDS, Donassollo TA, Henn Donassollo S, Demarco FF (2021) Impact of tooth bleaching on oral health-related quality of life in adults: A triple-blind randomised clinical trial. J Dent 105:103564. https://doi.org/10.1016/j.jdent.2020.103564
5. Martini EC, Favoreto MW, de Andrade HF, Coppla FM, Loguercio AD, Reis A (2021) One-year follow-up evaluation of reservoirs in bleaching trays for at-home bleaching. J Esthet Restor Dent 33:992–998. https://doi.org/10.1111/jerd.12797
6. Newton JT, Subramanian SS, Westland S, Gupta AK, Luo W, Joiner A (2021) The impact of tooth colour on the perceptions of age and social judgements. J Dent 112:103771. https://doi.org/10.1016/j.jdent.2021.103771
7. Haywood VB, Sword RJ (2021) Tray bleaching status and insights. J Esthet Restor Dent 33:27–38. https://doi.org/10.1111/jerd.12688
8. Kielbassa AM, Maier M, Gieren AK, Eliav E (2015) Tooth sensitivity during and after vital tooth bleaching: A systematic review on an unsolved problem. Quintessence Int 46:881–897. https://doi.org/10.3290/j.qi.a34700
9. Esteves L, Fagundes TC, Dos Santos PH, da Silva L, de Alcântara S, Cintra L, Briso A (2022) Does the Bleaching Gel Application Site Interfere With the Whitening Result? A Randomized Clinical Trial. Oper Dent 47:20–30. https://doi.org/10.2341/20-236-c
10. Mayer-Santos E, Bachiega-Silva B, Twiaschor CV, Shimokawa CAK, Marinho GB, Junior AB, Zanin F, Brugnera AP, Ramalho KM, de Freitas PM (2022) Blinded, parallel and randomized clinical evaluation of in-office dental bleaching with violet LED (405–410nm). Photodiagnosis Photodyn Ther 38:102739. https://doi.org/10.1016/j.pdpdt.2022.102739
11. Rodríguez-Martínez J, Valiente M, Sánchez-Martín MJ (2019) Tooth whitening: From the established treatments to novel approaches to prevent side effects. J Esthet Restor Dent 31:431–440. https://doi.org/10.1111/jerd.12519
12. Kury M, Wada EE, Silva DPD, Tabchoury CPM, Giannini M, Cavalli V (2020) Effect of violet LED light on in-office bleaching protocols: a randomized controlled clinical trial. J Appl Oral Sci 28:e20190720. https://doi.org/10.1590/1678-7757-2019-0720
13. Pontes M, Gomes J, Lemos C, Leão RS, Moraes S, Vasconcelos B, Pellizzer EP (2020) Effect of Bleaching Gel Concentration on Tooth Color and Sensitivity: A Systematic Review and Meta-analysis. Oper Dent 45:265–275. https://doi.org/10.2341/17-376-l
14. de Geus JL, Wambier LM, Boing TF, Loguercio AD, Reis A (2018) At-home Bleaching With 10% vs More Concentrated Carbamide Peroxide Gels: A Systematic Review and Meta-analysis. Oper Dent 43:E210-e222. https://doi.org/10.2341/17-222-l
15. Chemin K, Rezende M, Costa MC, Salgado A, de Geus JL, Loguercio AD, Reis A, Kossatz S (2021) Evaluation of At-home Bleaching Times on Effectiveness and Sensitivity with 10% Hydrogen Peroxide: A Randomized Controlled Double-blind Clinical Trial. Oper Dent 46:385–394. https://doi.org/10.2341/20-104-c
16. Al-Qunaian TA, Matis BA, Cochran MA (2003) In vivo kinetics of bleaching gel with three-percent hydrogen peroxide within the first hour. Oper Dent 28:236–241
17. Terra R, da Silva KL, Vochikovski L, Sutil E, Rezende M, Loguercio AD, Reis A (2021) Effect of Daily Usage Time of 4% Hydrogen Peroxide on the Efficacy and Bleaching-induced Tooth Sensitivity: A Single-blind Randomized Clinical Trial. Oper Dent 46:395–405. https://doi.org/10.2341/20-058-c
18. Cardoso PC, Reis A, Loguercio A, Vieira LC, Baratieri LN (2010) Clinical effectiveness and tooth sensitivity associated with different bleaching times for a 10 percent carbamide peroxide gel. J Am Dent Assoc 141:1213–1220. https://doi.org/10.14219/jada.archive.2010.0048
19. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, McKenzie JE (2021) PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ 372:n160. https://doi.org/10.1136/bmj.n160
20. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT (2019) RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 366:l4898. https://doi.org/10.1136/bmj.l4898
21. Higgins J, Thomas J (2022) Cochrane Handbook for Systematic Reviews of Interventions | Cochrane Training. Oxford: The Cochrane Collaboration. https://training.cochrane.org/handbook/current
22. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, Guyatt GH (2011) GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 64:401–406. https://doi.org/10.1016/j.jclinepi.2010.07.015
23. Pavani CC, Fagundes TC, Sundfeld D, Santin GC, Machado LS, Bertoz APM, Schott TC, Sundfeld RH (2023) Influence of daily usage times on patients' compliance during at-home bleaching: a randomized clinical trial. J Appl Oral Sci 31:e20230181. https://doi.org/10.1590/1678-7757-2023-0181
24. Pavani CC (2022) Analysis of different times of use of the bleaching gel in the effectiveness of home dental whitening: randomized clinical study of split-mouth. Dissertation, Sao Paulo State University (UNESP)
25. Mota LSB (2021) 6% hydrogen peroxide at home bleaching: efficacy, sensitivity and psychosocial impact at different application times – blind randomized clinical trial. Dissertation, Federal University of Amazonas
26. López Darriba I, Novoa L, de la Peña VA (2017) Efficacy of different protocols for at-home bleaching: A randomized clinical trial. Am J Dent 30:329–334
27. Carneiro JRM (2016) Randomized clinical trial on the different bleaching protocols with 7,5% hydrogen peroxide. Dissertation, Federal University of Ceara
28. Vochikovski L, Favoreto MW, Rezende M, Terra RMO, da Silva KL, Farago PV, Loguercio AD, Reis A (2023) Effect of an experimental desensitizing gel on bleaching-induced tooth sensitivity after in-office bleaching-a double-blind, randomized controlled

trial. Clin Oral Investig 27:1567–1576. https://doi.org/10.1007/s00784-022-04778-2
29. Rodrigues JL, Rocha PS, Pardim SLS, Machado ACV, Faria ESAL, Seraidarian PI (2018) Association Between In-Office And At-Home Tooth Bleaching: A Single Blind Randomized Clinical Trial. Braz Dent J 29:133–139. https://doi.org/10.1590/0103-6440201801726
30. Gonçalves MLL, Tavares A, Mota A, Penna LAP, Deana AM, Bussadori SK (2017) In-Office Tooth Bleaching for Adolescents Using Hydrogen Peroxide-Based Gels: Clinical Trial. Braz Dent J 28:720–725. https://doi.org/10.1590/0103-6440201701516
31. Cordeiro D, Toda C, Hanan S, Arnhold LP, Reis A, Loguercio AD, Bandeira MCL (2019) Clinical Evaluation of Different Delivery Methods of At-Home Bleaching Gels Composed of 10% Hydrogen Peroxide. Oper Dent 44:13–23. https://doi.org/10.2341/17-174-c
32. Igiel C, Weyhrauch M, Wentaschek S, Scheller H, Lehmann KM (2016) Dental color matching: A comparison between visual and instrumental methods. Dent Mater J 35:63–69. https://doi.org/10.4012/dmj.2015-006
33. Pérez Mdel M, Ghinea R, Rivas MJ, Yebra A, Ionescu AM, Paravina RD, Herrera LJ (2016) Development of a customized whiteness index for dentistry based on CIELAB color space. Dent Mater 32:461–467. https://doi.org/10.1016/j.dental.2015.12.008
34. Pérez MM, Herrera LJ, Carrillo F, Pecho OE, Dudea D, Gasparik C, Ghinea R, Bona AD (2019) Whiteness difference thresholds in dentistry. Dent Mater 35:292–297. https://doi.org/10.1016/j.dental.2018.11.022
35. Martini EC, Favoreto MW, Coppla FM, Loguercio AD, Reis A (2020) Evaluation of reservoirs in bleaching trays for at-home bleaching: a split-mouth single-blind randomized controlled equivalence trial. J Appl Oral Sci 28:e20200332. https://doi.org/10.1590/1678-7757-2020-0332
36. Forville H, Favoreto MW, Wendlinger M, Dias RM, Ferreira Borges CP, Reis A, Loguercio AD (2023) Evaluation of at-home bleaching protocol with application on different surfaces: bleaching efficacy and hydrogen peroxide permeability. Restor Dent Endod 48:e33. https://doi.org/10.5395/rde.2023.48.e33
37 Joiner A, Luo W (2017) Tooth colour and whiteness: A review. J Dent 67s:S3-s10. https://doi.org/10.1016/j.jdent.2017.09.006
38. Paravina RD (2008) New shade guide for tooth whitening monitoring: visual assessment. J Prosthet Dent 99:178–184. https://doi.org/10.1016/s0022-3913(08)60041-4
39. Paravina RD, Ghinea R, Herrera LJ, Bona AD, Igiel C, Linninger M, Sakai M, Takahashi H, Tashkandi E, Perez Mdel M (2015) Color difference thresholds in dentistry. J Esthet Restor Dent 27(Suppl 1):S1-9. https://doi.org/10.1111/jerd.12149
40. Muka T, Glisic M, Milic J, Verhoog S, Bohlius J, Bramer W, Chowdhury R, Franco OH (2020) A 24-step guide on how to design, conduct, and successfully publish a systematic review and meta-analysis in medical research. Eur J Epidemiol 35:49–60. https://doi.org/10.1007/s10654-019-00576-5
41. Kwon SR, Wertz PW (2015) Review of the Mechanism of Tooth Whitening. J Esthet Restor Dent 27:240–257. https://doi.org/10.1111/jerd.12152
42. Soares DG, Basso FG, Pontes EC, Garcia Lda F, Hebling J, de Souza Costa CA (2014) Effective tooth-bleaching protocols capable of reducing H(2)O(2) diffusion through enamel and dentine. J Dent 42:351–358. https://doi.org/10.1016/j.jdent.2013.09.001
43. de Almeida LC, Soares DG, Gallinari MO, de Souza Costa CA, Dos Santos PH, Briso AL (2015) Color alteration, hydrogen peroxide diffusion, and cytotoxicity caused by in-office bleaching protocols. Clin Oral Investig 19:673–680. https://doi.org/10.1007/s00784-014-1285-3
44. de Almeida LC, Soares DG, Azevedo FA, Gallinari Mde O, Costa CA, dos Santos PH, Briso AL (2015) At-Home Bleaching: Color Alteration, Hydrogen Peroxide Diffusion and Cytotoxicity. Braz Dent J 26:378–383. https://doi.org/10.1590/0103-6440201300380
45. Mena-Serrano AP, Parreiras SO, do Nascimento EM, Borges CP, Berger SB, Loguercio AD, Reis A (2015) Effects of the concentration and composition of in-office bleaching gels on hydrogen peroxide penetration into the pulp chamber. Oper Dent 40:E76-82. https://doi.org/10.2341/13-352-l