UNIVERSIDADE ESTADUAL DO OESTE DO PARANÁ
CENTRO DE CIÊNCIAS BIOLÓGICAS E DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM
ODONTOLOGIA (PPGO) - MESTRADO

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Quality of life assessment in patients undergoing at-home tooth whitening – systematic review and meta-analysis

Cascavel-PR
2022

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Dissertação apresentada ao Programa de Pós-Graduação em Odontologia, Centro de Ciências Biológicas e da Saúde, Universidade Estadual do Oeste do Paraná, como requisito parcial para obtenção do título de Mestre em Odontologia Área de concentração: Odontologia Orientadora: Prof. Dra. Fabiana Scarparo Naufel e coorientador: Prof. Dra. Bianca Medeiros Maran

Área de concentração: Odontologia (Materiais Odontológicos)

Orientadora: Prof. Dra. Fabiana Scarparo Naufel

Coorientador: Prof. Dra. Bianca Medeiros Maran

Cascavel-PR

2022

Ficha de identificação da obra elaborada através do Formulário de Geração Automática do Sistema de Bibliotecas da Unioeste.

CENCI MATICK ROMBALDO, ANNA CAROLINA
Quality of life assessment in patients undergoing at-home tooth whitening ? systematic review and meta-analysis / ANNA CAROLINA CENCI MATICK ROMBALDO; orientadora FABIANA SCARPARO NAUFEL; coorientadora BIANCA MEDEIROS MARAN. -- Cascavel, 2022.
47 p.

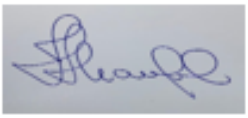
Dissertação (Mestrado Acadêmico Campus de Cascavel) -- Universidade Estadual do Oeste do Paraná, Centro de Ciências Biológicas e da Saúde, Programa de Pós-Graduação em Odontologia, 2022.

1. QUALIDADE DE VIDA. 2. CLAREAMENTO DENTAL. 3. DENTES DESCOLORIDOS. I. SCARPARO NAUFEL, FABIANA, orient. II. MEDEIROS MARAN, BIANCA, coorient. III. Título.

ANNA CAROLINA CENCI MATICK ROMBALDO

Avaliação da qualidade de vida em pacientes submetidos ao clareamento dental caseiro - revisão sistemática e metanálise

Dissertação apresentada ao Programa de Pós-Graduação em Odontologia em cumprimento parcial aos requisitos para obtenção do título de Mestra em Odontologia, área de concentração Odontologia, linha de pesquisa Materiais Dentários Aplicados à Clínica Odontológica, APROVADO(A) pela seguinte banca



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Cascavel, 25 de fevereiro de 2022.

DEDICATÓRIA

Dedico essa dissertação à minha mãe, por ter sido meu maior incentivo a continuar na área acadêmica, sendo sempre um grande exemplo de dedicação e minha maior inspiração como pessoa.

AGRADECIMENTOS

A Deus, por sempre me permitir trilhar os planos Dele, que continuam infinitamente maiores e melhores que os meus, me sustentando e capacitando em todos os momentos.

A minha família, por terem sido mais uma vez meu porto seguro e meu apoio e por sempre me incentivarem a seguir e viver os meus sonhos.

A meu marido, por não medir esforços para que mais uma etapa fosse realizada, me apioando incondicionalmente em todos os momentos, e por ser uma grande inspiração de persistência e dedicação.

As minhas amadas orientadoras, profa Fabiana Naufel e profa Bianca Maran, por deixarem tudo mais leve e suave e me transmitirem tantas lições que levarei para sempre. Serão meus grandes exemplos de mestres.

A minha banca querida, profa Juliana Bombonatti e profa Eloisa Andrade, por compartilharem esse momento tão importante e especial e contribuírem para o meu crescimento.

A todos os mestres que passaram pela minha vida nessa etapa, minha gratidão pelo carinho e dedicação que tiveram, saibam que todo o aprendizado e convivência fizeram muita diferença na minha vida.

A minha amiga especial, Larissa Pozzobon, que levarei por toda a vida, agradeço por compartilhar comigo dos melhores e mais difíceis momentos ao longo dessa jornada, deixando-a mais alegre e bonita.

Aos meus colegas e à Unioeste, que me acolheu por dois anos, muito obrigada por tantas experiências, guardarei em um lugar muito especial do meu coração.

Avaliação da qualidade de vida em pacientes submetidos a clareamento dental caseiro – revisão sistemática e metanálise

RESUMO

INTRODUÇÃO: O clareamento dental caseiro proporciona benefícios estéticos aos pacientes e pode ajudar a melhorar sua autoestima e autoconfiança. É também um tratamento simples e eficaz com ótimos resultados a curto prazo. Embora possa apresentar alguns riscos, é considerado um método seguro e minimamente invasivo. **OBJETIVO:** Avaliar, por meio de revisão sistemática e metanálise, se os pacientes submetidos ao clareamento dental caseiro tiveram sua qualidade de vida melhorada. **MATERIAIS E MÉTODO:** Os estudos foram pesquisados nas seguintes bases de dados eletrônicas (até junho de 2021): MEDLINE (via PubMed), Biblioteca Cochrane, Biblioteca Odontológica Brasileira, Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) e bases de citações (Scopus, Web of Science e EMBASE). Os estudos foram selecionados de acordo com seus títulos, sem restrições de idioma. A qualidade do estudo foi avaliada com a ferramenta Cochrane Collaboration para detectar o risco de viés. **TRATAMENTO ESTATÍSTICO:** Os dados foram analisados com o software estatístico RStudio e resumidos calculando a diferença média padronizada para dados contínuos e razão de risco e, juntamente com o intervalo de confiança de 95%, para dados dicotômicos, usando um modelo de efeitos aleatórios expresso em tabelas e gráficos. **RESULTADOS:** Duplicatas foram removidas e dois revisores selecionaram os estudos que atendiam aos critérios de inclusão. Dos 68 artigos em texto completo avaliados, 13 permaneceram e foram analisados para resultados iniciais. Destes, um artigo teve alto risco de viés, um teve baixo risco e os outros 11 tiveram risco incerto. Dos 13 artigos avaliados, sete fizeram parte da metanálise e apresentaram 87% de satisfação do paciente após o clareamento. **CONCLUSÃO**: Houve melhora na qualidade de vida dos pacientes submetidos ao clareamento dental caseiro.

PRÓSPERO: CRD42020220354

Palavras-chave: Qualidade de vida, Clareamento dentário, Descoloração dentária.

Quality of life assessment in patients undergoing at-home tooth whitening – systematic review and meta-analysis

ABSTRACT

INTRODUCTION: At-home tooth bleaching provides esthetic benefits to patients and can help to improve their self-esteem and self-confidence. It is also a simple and effective treatment with great short-term results. Although it may present some risks, it is considered a safe and minimally invasive method. **OBJECTIVE:** To assess, through a systematic review and meta-analysis, whether patients subjected to at-home tooth bleaching had their quality of life improved. **MATERIALS AND METHOD:** The studies were searched in the following electronic databases (until June 2021): MEDLINE (via PubMed), Cochrane Library, Brazilian Dental Library, Latin American and Caribbean Literature on Health Sciences (LILACS), and citation databases (Scopus, Web of Science and EMBASE). The studies were selected according to their titles, without language restrictions. Study quality was assessed with the Cochrane Collaboration tool to detect the risk of bias. **STATISTICAL TREATMENT:** The data was analyzed with the RStudio statistical software and summarized by calculating the standardized mean difference for continuous data and risk ratio and, along with the 95% confidence interval, for dichotomous data, using a random-effects model expressed in tables and graphs. **RESULTS:** Duplicates were removed and two reviewers selected the studies that met the inclusion criteria. Of the 68 full-text articles evaluated, 13 remained and were analyzed for initial results. Of these, one article had a high risk of bias, one had a low risk, and the other 11 had an uncertain risk. Of the 13 articles evaluated, seven were part of the meta-analysis and presented 87% of patient satisfaction after bleaching. **CONCLUSION:** There was an improvement in the quality of life of patients subjected to at-home tooth bleaching.

PROSPERO: CRD42020220354

Keywords: Quality of life, Tooth bleaching, Tooth discoloration.

ABBREVIATION LIST

BA	Bleaching Agent
AR	High Risk
LR	Low Risk
AH	At- Home Bleaching
IN	In- Office whitening
OHIP	Oral Health Impact Profile for Dental Aesthetics
PIDAQ	Psychosocial Impact of the Dental Aesthetics Questionnaire
OES	Oralfacial Esthetic Scale
EEO	Escala de Estética Oral
WD	Whitening Dentifrices
SMD	Standardized Mean Difference
SD	Standard Deviation
NRS	Numerical Rating Scale
RCT	Randomized Clinical Study
AVS	Analog Visual Scale
CI	Confidence Interval
ID	Identification
GI	Gingival Irritation
n.r.	Not Reported in the Study
CP	Carbamide Peroxide
HP	Hydrogen Peroxide
IR	Uncertain risk
RoB	Risk of Bias
PS	Patient Satisfaction
Vs.	*Versus*

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Dissertação elaborada e formatada conforme as normas das publicações científicas: Journal of Dentistry
Disponível em:
https://www.elsevier.com/wps/find/journaldescription.cws_home/30441?generatepdf=true

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CAPÍTULO 1

Quality of life assessment in patients undergoing at-home tooth whitening – systematic review and meta-analysis

Introduction

Overall, the search for esthetics has been increasingly evidenced in society and this search is not different in dentistry, as esthetic treatments are frequently required by patients. Tooth bleaching, regardless of the form of application, consists of a conservative esthetic treatment because it improves smile appearance and preserves the tooth structure (NASCIMENTO et al., 2018).

In summary, there are two bleaching techniques: at-home and in-office. In-office bleaching is performed with high concentrations of hydrogen peroxide or carbamide peroxide gel (ALQAHTANI, 2014) and at-home bleaching is performed by the patients with the supervision of the dentist. In the latter technique, the main choices of bleaching gels are 10% to 22% carbamide peroxide and 3% to 10% hydrogen peroxide (ALQAHTANI, 2014) (MOKHLIS et al., 2000) (BIZHANG et al., 2009) (GHALILI et al., 2014) (ALONSO DE LA PENA V. & LOPEZ RATON M., 2014).

Although tooth bleaching, regardless of the technique, may cause some adverse effects such as tooth sensitivity (REIS et al., 2011) (TAY et al., 2012) (He LB et al., 2012) (BONAFÉ et al., 2013), the assessment of the benefits of this procedure imply that the improvement in dental esthetics results in physical and self-esteem improvements (BARBIERE; RAPOPORT, 2009).

Job opportunities, personal relationships, and personality assessments are directly related to the pleasant appearance of teeth (BERSEZIO et al., 2018). However, when patients are dissatisfied with their appearance, they may show insecurity, low esteem, and anxiety, as well as physical and mental problems (NASCIMENTO et al., 2018).

Considering that clinical indicators cannot measure the social impacts on the lives of patients due to their subjectivity, quality of life assessment tools are used. An example is the Oral Health Impact Profile (OHIP), initially composed of 49 items and later simplified to 14, which focus on assessing functional limitations, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and social disadvantage (ALVARENGA et al., 2011). There are also other widely used questionnaires: the PIDAQ, which assesses the psychosocial impacts of esthetics on the quality of life of patients, created by KLAGES et al. (2006), and composed of items including domains and subdomains such as self-confidence, social and psychological impacts, and esthetic concern; and the OES (Orofacial Esthetic Scale), which can be used with the same objective to assess the esthetic perception of patients and consists of eight

items involving esthetic aspects of the face, teeth, and gums, and one question for the overall assessment of the face and mouth (BONAFÉ, 2016). These questionnaires can be applied alone or combined.

Although some studies have assessed the impact of at-home tooth bleaching on the quality of life of patients, the literature does not present a systematic review aiming to find the true impact of this treatment on the lives of patients.

Objective

Therefore, the present study aims to assess, with a systematic review and meta-analysis, whether patients subjected to at-home tooth bleaching had their quality of life improved.

Methodology

Protocol and registration

This systematic review was registered in the international prospective register of systematic reviews (PROSPERO) under number CRD42020220354 and followed the preferred reporting items for systematic review and meta-analysis protocols (PRISMA) recommendations (PAGE et al., 2021).

Information sources and search strategy

The search strategy (Table 1) was initially defined for the MEDLINE via PubMed database, considering a controlled vocabulary (MeSH terms) and free keywords for each concept of the PICO question described at the end of the introduction. The outcomes assessed were the changes in the quality of life of patients subjected to at-home tooth bleaching, using specific questionnaires.

The MEDLINE search strategy was adapted to other electronic databases (Cochrane Library, Brazilian Dental Library, Latin American and Caribbean Literature on Health Sciences (LILACS)), and citation databases (Scopus, Embase, and Web of Science) Moreover, the gray literature (SIGLE) was investigated by searching the abstracts of the annual conference of the International Association for Dental Research (IADR) and its regional divisions (2001-2021), the System for Information on Grey Literature database in Europe, dissertations and theses using the ProQuest Dissertations and Theses full-text database, and the Capes Theses journal database. The ongoing studies were searched in the following clinical trial registers: Current Controlled Trials, International Clinical Trial Registry Platform, ClinicalTrials.gov, Rebec, and EU Clinical Trials Register.

Moreover, the lists of references of all primary and eligible studies of this systematic review were searched manually for additional relevant publications. The first two pages of study links related to each primary study in the PubMed database were also reviewed to search for eligible studies. In the entire search process, the studies were restricted based on publication date (June 7, 2021) and without language restrictions.

TABLE 1. ELECTRONIC DATABASE AND SEARCH STRATEGY INITIALLY CONDUCTED ON APRIL 14, 2021 (UPDATED ON JUNE 22, 2021)

Pubmed (April 15, 2021)		
#1 ((((((((((((((((((((Tooth discoloration[MeSH Terms]) OR ("Tooth discoloration"[Title/Abstract])) OR (Color[MeSH Terms])) OR ("tooth discolouration"[Title/Abstract])) OR ("teeth discoloration"[Title/Abstract])) OR ("teeth discolouration"[Title/Abstract])) OR ("discolored tooth"[Title/Abstract])) OR ("discoloured tooth"[Title/Abstract])) OR ("discolored 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]))) OR (colour[Title/Abstract])	**#2** ((((((((((((((((((((((Quality of Life[MeSH Terms]) OR ("Quality of Life"[Title/Abstract])) OR ("Oral Health"[Title/Abstract])) OR (Oral Health[MeSH Terms])) OR (Quality of Health Care[MeSH Terms])) OR ("Quality of Health Care"[Title/Abstract])) OR ("Life Quality"[Title/Abstract])) OR (Tooth Bleaching[MeSH Terms]))) OR (Tooth Bleaching Agents[MeSH Terms])) OR (Hydrogen Peroxide[MeSH Terms]))) OR ("Hydrogen Peroxide"[Title/Abstract])) OR ("Carbamide Peroxide"[Title/Abstract])) OR (Carbamide Peroxide[MeSH Terms])) OR (dental offices[MeSH Terms]))) OR ("Dental Offices"[Title/Abstract])) OR ("At-home"[Title/Abstract])) OR ("In-office"[Title/Abstract])) OR (Bleaching[Title/Abstract])) OR (Whitening[Title/Abstract])) OR ("dentist-supervised"[Title/Abstract]))	**#3** (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR ("clinical trial"[tw]) OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR (placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR comparative study[pt] OR evaluation studies as topic[mh] OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospective*[tw] OR volunteer*[tw]) NOT (animals[mh] NOT humans[mh]))
#1 AND #2 AND #3		
Cochrane (May 22, 2021)		
#1 Mesh Descriptor: [Tooth Discoloration] explode all trees #2 Mesh Descriptor: [Color] explode all trees #3 (discolored next t*th): ti,ab,kw OR (color): ti,ab,kw OR (discolored next t*th): ti,ab,kw OR (dental next discoloration): ti,ab,kw OR (t*th next staining): ti,ab,kw #4 (stained t*th): ti,ab,kw OR (dental next staining): ti,ab,kw #5 #1 or #2 or #3 or #4	#6 Mesh Descriptor: [Quality of Life] explode all trees #7 Mesh Descriptor: [Oral Health] explode all trees #8 Mesh Descriptor: [Quality of Health Care] explode all trees #9 Mesh Descriptor: [Tooth Bleaching] explode all trees #10 Mesh Descriptor: [Tooth Bleaching Agents] explode all trees #11 Mesh Descriptor: [Hydrogen Peroxide] explode all trees #12 Mesh Descriptor: [Carbamide Peroxide] explode all trees #13 Mesh Descriptor: [Dental offices] explode all trees #14 ("quality of life"): ti,ab,kw OR ("oral health"): ti,ab,kw OR ("quality of health care") ti,ab,kw OR (t*th next bleaching): ti,ab,kw OR ("life quality"): ti,ab,kw #15 ("hydrogen peroxide"): ti,ab,kw OR ("carbamide peroxide") ti,ab,kw OR ("dental offices") ti,ab,kw OR ("at-home"): ti,ab,kw OR ("in-office"): ti,ab,kw #16 (bleaching): ti,ab,kw OR (whitening) ti,ab,kw OR ("dentist-supervised") ti,ab,kw #17 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16	
#18 #5 AND #17		
Lilacs/BDL (May 12, 2021)		
#1 (MH: "Tooth discoloration" OR MH: color OR "Tooth discoloration" OR color OR "tooth discolouration" OR "teeth discoloration" OR "teeth discolouration" OR "discolored tooth" OR	**#2** (MH: "Quality of Life" OR MH: "Oral Health" OR MH: "Quality of Health Care" OR MH: "Tooth Bleaching" OR MH: "Tooth Bleaching Agents" OR MH: "Hydrogen Peroxide" OR MH:	

"discoloured tooth" OR "discolored teeth" OR "discoloured teeth" OR "dental discoloration" OR "dental discolouration" OR "dental discolouration" OR "tooth staining" OR "teeth staining" OR "stained tooth" OR "stained teeth" OR "dental staining" OR colour OR "descoloração dos dentes" OR "descoloração do dente" OR "dente descolorido" OR "dentes descoloridos" OR "descoloração dentária" OR "manchas nos dentes" OR "dente manchado" OR "dentes manchados" OR "coloração dentária" OR cor OR "decoloración del diente" OR "diente descolorido" OR "mancha del diente" OR "diente manchado" OR "manchado del diente" OR color)	"Carbamide Peroxide" OR MH: "dental offices" OR "Quality of Life" OR "Oral Health" OR "Quality of Health Care" OR "Life Quality" OR "Tooth Bleaching" OR "Tooth Bleaching Agents" OR "Hydrogen Peroxide" OR "Carbamide Peroxide" OR "Dental Offices" OR "At-home" OR "In-office" OR Bleaching OR Whitening OR "dentist-supervised" OR "Qualidade de vida" OR "Saúde bucal" OR "Qualidade dos cuidados de saúde" OR "Clareamento dentário" OR "Agentes clareadores dentais" OR "Peróxido de hidrogênio" OR "Peróxido de carbamida" OR "Consultórios odontológicos" OR "Em casa" OR "No consultório" OR Clareamento OR "supervisionado por dentista" OR "Calidad de vida" OR "Salud bucal" OR "Calidad de la atención médica" OR "Blanqueamiento dental" OR "Agentes blanqueadores de hidrógeno" OR "Peróxido de hidrógeno" OR "Consultorios dentales" OR "En casa" OR "En el consultorio" OR Blanqueamiento OR "supervisado por un dentista")
#1 AND #2	
Scopus (June 15, 2021)	
#1 (TITLE-ABS-KEY ("t??th discoloration") OR TITLE-ABS-KEY (Colo?r) OR TITLE-ABS-KEY ("t??th discolouration") OR TITLE-ABS-KEY ("discolored t??th") OR TITLE-ABS-KEY ("discoloured t??th") OR TITLE-ABS-KEY ("dental discolo?ration") OR TITLE-ABS-KEY ("t??th staining") OR TITLE-ABS-KEY ("stained t??th") OR TITLE-ABS-KEY ("dental staining"))	**#2** (TITLE-ABS-KEY ("Quality of Life") OR TITLE-ABS-KEY ("Oral Health") OR TITLE-ABS-KEY ("Quality of Health Care") OR TITLE-ABS-KEY ("Life Quality") OR TITLE-ABS-KEY ("Hydrogen Peroxide") OR TITLE-ABS-KEY ("Carbamide Peroxide") OR TITLE-ABS-KEY ("Dental Offices") OR TITLE-ABS-KEY ("At-home") OR TITLE-ABS-KEY ("In-office") OR TITLE-ABS-KEY (Bleaching) OR TITLE-ABS-KEY (Whitening) OR TITLE-ABS-KEY ("dentist-supervised"))
#1 AND #2	
Web of science (June 2, 2021)	
#1 TÓPICO:("t*th discolo*ration") OR TÓPICO:(colo$r) OR TÓPICO: ("discolo*red t*th") OR TÓPICO: ("dental discolo*ration") OR TÓPICO: ("t*th staining") OR TÓPICO: ("stained t*th") OR TÓPICO: ("dental staining")	**#2** TÓPICO:("quality of life") OR TÓPICO: ("oral health") OR TÓPICO: ("quality of health care") OR TÓPICO:("t*th bleaching") OR TÓPICO: ("life quality") OR TÓPICO: ("hydrogen peroxide") OR TÓPICO: ("carbamide peroxide") OR TÓPICO: ("dental offices") OR TÓPICO: ("at-home") OR TÓPICO: ("in-office") OR TÓPICO: (bleaching) OR TÓPICO: (whitening) OR TÓPICO: ("dentist-supervised")
#1 AND #2	
Embase (June 28, 2021)	
#1 'tooth discoloration'/exp OR 'color'/exp OR color: ab, ti OR 'tooth discoloration': ab, ti OR 'teeth discoloration': ab, ti OR 'teeth discoulouration': ab, ti OR 'discolored tooth': ab, ti OR 'discoloured tooth': ab, ti OR 'discoloured teeth': ab, ti OR 'discolored teeth': ab, ti OR 'tooth staining': ab, ti OR 'teeth staining': ab, ti OR 'stained tooth': ab, ti OR 'stained teeth': ab, ti OR 'dental staining' ab, ti	**#2** 'quality of life'/exp OR 'health'/exp OR 'health care quality'/exp OR 'quality of life': ab, ti OR 'dental procedure'/exp OR 'tooth bleaching agent'/exp OR 'hidrogen peroxide'/exp OR 'carbamide peroxide'/exp OR 'dental facility'/exp OR 'at home': ab, ti OR 'in office': ab, ti OR bleaching: ab, ti OR withening: ab, ti OR 'dentist supervised': ab, ti

Selection criteria

Randomized clinical trials assessing the quality of life of patients subjected to at-home tooth bleaching were included. Only parallel and split-mouth human clinical trials were included. The studies excluded were non-controlled clinical trials, editorial letters, case reports, and case series.

Selection of studies and data collection process

The studies selected in the bibliographical search were reviewed in three phases. All studies were initially analyzed with the help of the Endnote X6 software for relevance by title, then by abstracts, and, finally, a full-text assessment. If there were doubts in any of these phases, the study was forwarded to the next phase. Three reviewers read the full texts to verify the inclusion criteria.

Each eligible study received an identification (ID), combining the first author and year of publication. Two reviewers (LP/ACCM) independently summarized and categorized the data as study design, the number of patients, interventions, and results. In the case of disagreements, the decision was made by consulting with a third reviewer. If there were several reports of the same study (i.e., reports with different follow-ups), the data of all reports were extracted directly to one single data collection form to prevent multiple entries.

The data collected regarded quality of life improvement after concluding the bleaching treatment, with periods from seven to 30 days after bleaching. This variation occurred due to the differences in the assessment periods reported in the primary studies. If the study reported several assessments, the data were collected around seven days after bleaching because it was the most reported period. If the study assessed color change at least 360 days after bleaching, it was collected to assess the long-term efficacy of the study groups.

Data extraction and conversion to the desired format

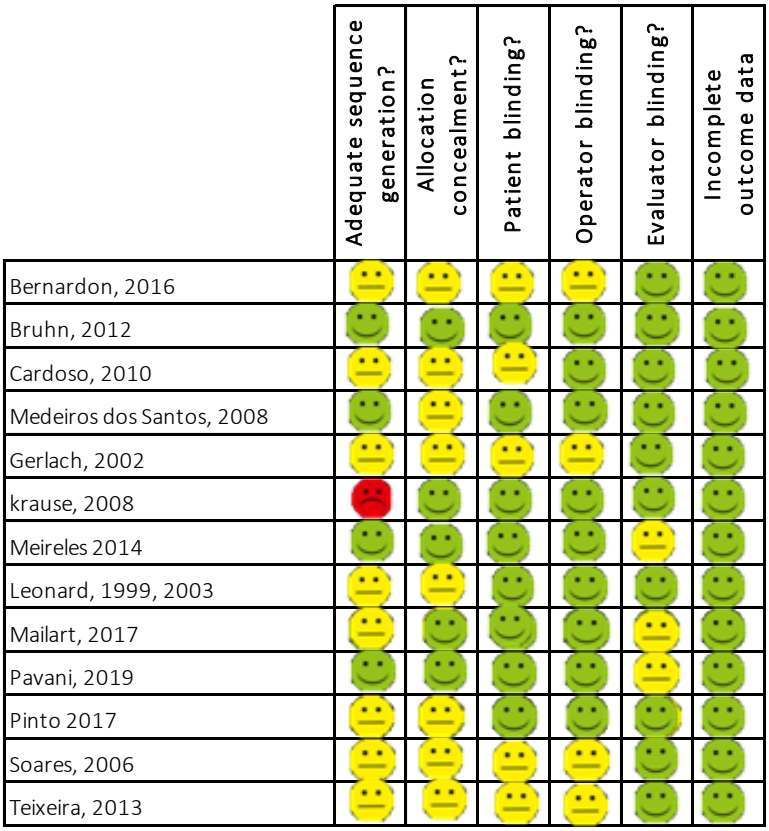
The data on patient satisfaction were extracted according to the reports of the primary studies.

Risk of bias of individual studies

Two independent reviewers assessed the quality of the trials selected with the Cochrane[21] collaboration tool to assess the risk of bias (version 1 of RoB) for randomized clinical trials. The assessment criteria had six items: selection bias (production of adequate sequence and allocation concealment), performance bias (patient and operator blinding), detection bias (evaluator blinding), attrition bias (incomplete result data), report bias (selective result data), and other biases. Any other type of bias in the last item of this systematic review was not included. The disagreements between the reviewers were solved with a discussion and, if necessary, by consulting with a third reviewer (B.M.M.).

Each item was classified as a low, high, or uncertain risk of bias. The study had a low risk of bias if all five items of the risk of bias tool had a low risk of bias. If one or more items were considered an uncertain risk, the study was considered an uncertain risk. If at least one item presented a high risk of bias, the study was considered a high risk of bias.

Figure 1. Summary of the assessment of the risk of bias according to the Cochrane collaboration tool.



Summarized measures and synthesis of results

The data were analyzed with the RStudio statistical software (Version 1.3.959 TM 2009-2020 RStudio, PBC). The meta-analysis was performed with all the eligible studies using the random-effects model and studies assessing the quality of life of patients after at-home bleaching.

Results

Selection of studies

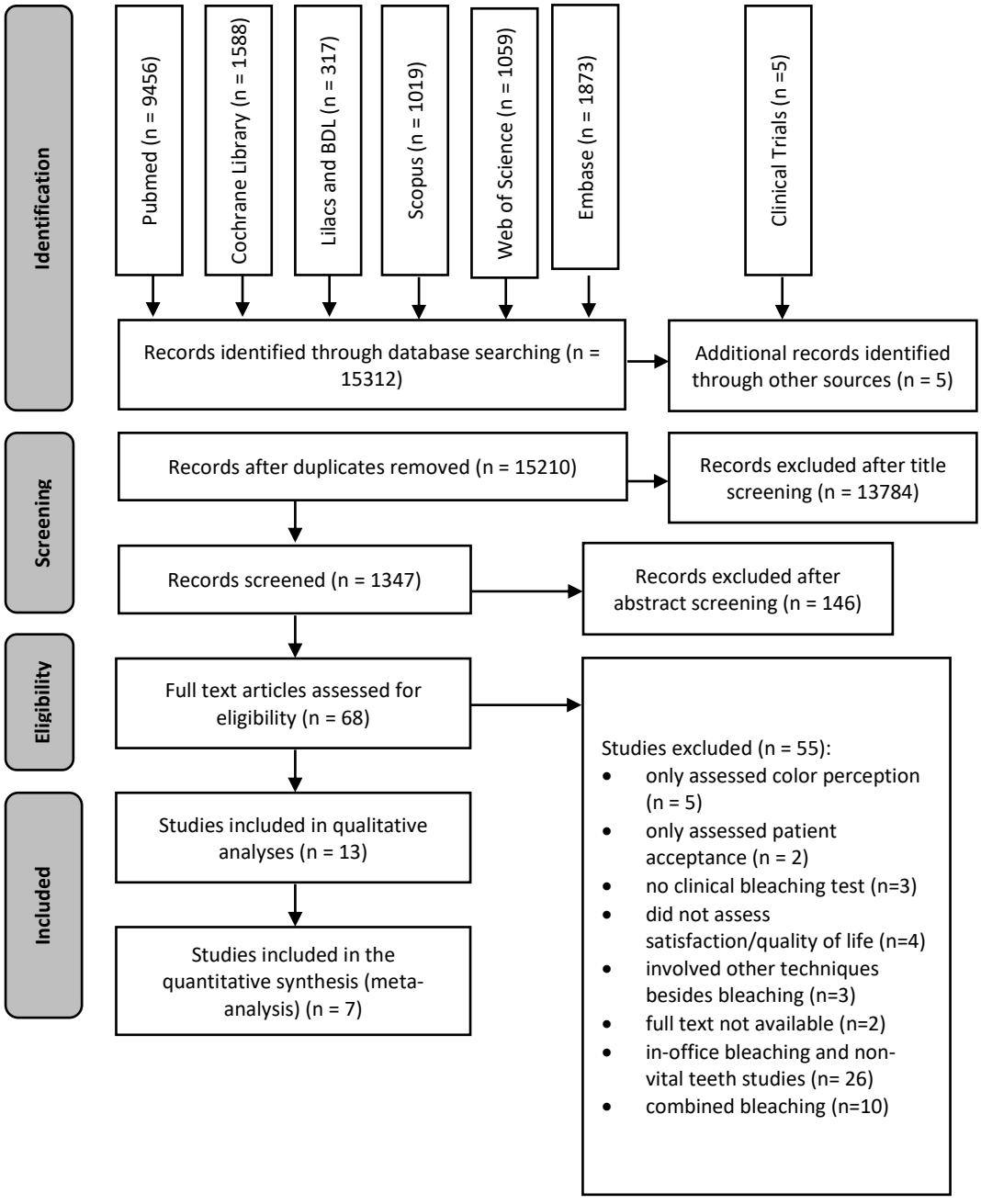
The search strategy was performed on April 14, 2021. After screening the databases and removing duplicates, 15,312 studies were identified. After the screening of duplicates, titles, and abstracts, 68 studies remained. The full texts of these 68 studies

were assessed and 66 randomized clinical trials were excluded for the following reasons: 26 studies assessed in-office bleaching and/or non-vital tooth bleaching, 10 assessed combined bleaching, 11 did not assess patient satisfaction, three were not clinical studies, two did not have full texts available, and three involved other bleaching techniques (Figure 2).

Characteristics of the studies included

Chart 1 lists the characteristics of the 13 eligible studies. Twelve studies were parallel, and only one was a split-mouth study. The age of patients ranged from 18 to 50 years (Chart 1).

Figure 2. Flowchart of study identification.



Study identification	Study design [Setting]	Number of patients	Average age of subjects ± SD [interval]	Number of men (%)	Base color/tooth assessed	HP/CP concentration (%)/number of patients per group	Application protocol	Quality of life assessment tool	Follow-up
Bernardon 2016[15]	Split-mouth [n.r.]	50	n.r. +- n.r. [18-40]	n.r. [n.r.]	A_2/upper anterior teeth	G1: 10% CP opalescence (right) + 10% CP power bleaching (left) G2: 15% CP opalescence (right) + 16% CP power bleaching (left)	2 hours a day for 45 days	Form in each appointment (satisfied/dissatisfied)	15 pt [50] 30 pt [50] 45 pt [50] 180 pt [n.r.]
Bruhn 2012[16]	Parallel [university]	62	n.r. +- n.r. [>50]	25 [40.32]	n.r./anterior teeth	Bleaching agent: 14% HP/31 Placebo: without bleaching agent/31	2x a day for 3 weeks	AQS OHIP	0 pt [62] 21 pt [n.r.] 90 pt [53]
Cardoso 2010[17]	Parallel [university]	60	n.r. [17-30]	n.r. [n.r.]	A_2/upper central incisors	G1: 10% CP for 15 minutes G2: 10% CP for 30 minutes G3: 10% CP for 1 hour G4: 10% CP for 8 hours	G1: 15 minutes a day for 16 days or until satisfied G2: 30 minutes a day for 16 days or until satisfied G3: 60 minutes a day for 16 days or until satisfied G4: 480 minutes a day for 16 days or until satisfied	Questionnaires	0 pt [60] 16 pt [60]

Dos Santos Medeiros 2008[18]	Parallel [university]	50	21.6 +-1.7 [18-25]	15 [30%]	n.r./upper incisors	G1: 10% CP/ 25 G2: Placebo/ 25	Every night for 21 days	Questionnaires	0 pt [50] 21 pt [50] 30 pt [50] 180 pt [50]
Gerlach 2002 [19]	Parallel [university]	50	G1: 32.9 [9.66] 18-53 G2: 31.7 [8.83] 19-49	G1: 1 [4%] G2: 6 [24%]	n.r./anterior teeth	G1: 3% HP/25 G2: 6%/ 25	G1: 10 to 20 minutes a day for 7 days [double arch impression tray] G2: 30 minutes a day for 14 days [flexible strips]	0-5 scale	0 pt [50] 7 pt [50] 14 pt [50]
Krause 2008 [20]	Parallel [n.r.]	30	31 (+-4) [n.r. – n.r.]	16 [53.3%]	n.r./n.r.	G1: 10% CP/10 G2: 17% CP/10 G3: PLACEBO/ 10	2 hours a day for 7 days	Intermodal intensity comparison	0 pt [30] 1 pt [30] 2 pt [30] 3 pt [30] 4 pt [30] 7 pt [30]
Leonard 1993, 2003 [21]	Parallel [university]	15	>18	n.r.	Teeth with tetracycline/ upper anterior incisors	10% CP	At night	Questionnaires	180 pt [13] 360 pt [13] 1620 pt [12] 2700 pt [15]

Mailart 2017 [22]	Parallel [university]	45	[18- n.r.]	n.r. [n.r.]	A_2 or higher/ upper anterior teeth	G1: 10% HP/15 (STANDARD) G2: 10% HP/15 (CUSTOMIZED) G3: 10% CP/15 (CUSTOMIZED)	G1: 30 minutes a day for 14 days G2: 30 minutes a day for 14 days G3: 2 hours a day for 14 days	OIDP	0 pt [n.r.] 90 pt [n.r.] 180 pt [n.r.]
Meireles 2014[23]	Parallel [n.r.]	92	45 [48.9] 18-20 47 [51.1] 21-30	31 [33.7]	C_1 or higher/ upper anterior teeth	G1: 16% CP/ 46 G2: 10% CP/ 46	2 hours a day for 3 weeks	OIDP	0 pt [92] 7 pt [91]
Pavani 2019 [24]	Parallel [university]	66	[18 - 22]	n.r. [n.r.]	A_2/ incisors and canines	10% CP/ 66	2 hours a day for 21 days/22 4 hours a day for 21 days/22 8 hours a day for 21 days/22	VAS	0 pt [n.r.] 7 pt [n.r.] 14 pt [n.r.] 21 pt [n.r.] 14 pt [n.r.]
Pinto 2017 [25]	Parallel [university]	42	16 [14-27] 17.5 [14-25] 16 [13-19] 17 [13-27]	24 [57.24]	Incisors and canines	G1: 10% HP/10 G2: 7.5% HP/10 G3: 6% HP/10 PLACEBO/12	30 minutes 2x day for 7 days 1 hour a day for 7 days 1 hour a day for 7 days 1 hour a day for 7 days	Questionnaires	7 pt [n.r.] 30 pt [n.r.] 180 pt [n.r.] 360 pt [n.r.]
Soares 2006 [26]	Parallel [university]	40	n.r. [n.r.]	21 [52.5]	n.r.	G1: 10% CP manipulated/ 20 G2: 10% CP industrialized/ 20	4/5 hours per night for 14 days	Spontaneous response	7 pt [n.r.] 14 pt [40] 30 pt [n.r.]

Teixeira 2013 [27]	Parallel [university]	75	[n.r. - 30]	32 [42.6]	n.r./ upper anterior incisors	16% CP/ 75	6 hours per night for 21 days	OHIP and ROSENBERG self-esteem scale	0 pt [75] 7 pt [74] 14 pt [72] 21 pt [63] 30 pt [51]

Chart 1 – Summary of the primary studies included in the systematic review.

Acronyms: SD= standard deviation; HP= hydrogen peroxide; CP= carbamide peroxide; n.r.= not representative; G1= group 1; G2= group 2; G3= group 3; G4= group 4; pt= post-treatment days; AQS= additional questions survey; OHIP= Oral Health Impact Profile For Dental Aesthetics; OIDP= Oral Impacts on Daily Performances; VAS= visual analog scale.

Quality of life

ESTUDO	MÉTODO DE AVALIAÇÃO UTILIZADO
- Cardoso 2010 - Dos Santos Medeiros 2008 - Leonard 1993, 2003 - Pinto 2017	- Questionários, sem especifica-los
- Soares 2006	- Resposta espontânea
- Mailart 2017 - Meireles 2014	- Impacto Oral no Desempenho Diário (OIDP)
- Gerlach 2002	- Escala de 0-5
- Bernardon 2016	- Formulário, sem especificá-lo
- Krause 2008	- Comparação da intensidade estimada.
- Pavani 2019	- Escala visual analógica (EVA) 0-10
- Bruhn 2012	- AQS, OHRQOL e OHIP juntos
- Teixeira 2013	- OHIP e o questionário de autoestima de Rosemberg

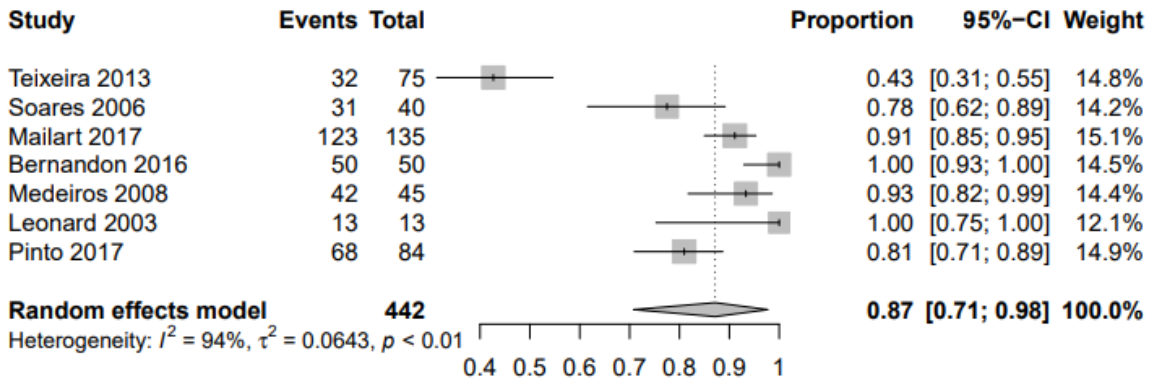
Chart 2 - Assessment methods.

Bleaching protocols

The bleaching gels used for at-home bleaching were CP and HP. Nine studies[15,23,27,28,24,21,17,18,20] used CP in concentrations between 10% and 17% and the daily use time varied between 15 minutes and eight hours. Four studies[16,27,19,22] used HP, which presented a concentration between 3% and 10%, with daily gel use between 10 and 60 minutes at an interval from seven to 21 days.

Meta-analysis

Figure 3. Meta-analysis result.



Of all the eligible studies, six could not enter the meta-analysis due to the lack of data reporting, and the seven studies included reported patient satisfaction with dichotomous data, assessing the relationship of at-home tooth bleaching and quality of life.

The improvement evidence in this interaction was 87.0% (95% CI: 31.0-100.0; I^2 = 94.0%). The lowest evidence found was 43.0% in the study by Teixeira (2013), while the highest was 100% in the studies by Leonard (2003) and Bernardon (2016) (Figure 3).

Discussion

The results obtained in the meta-analysis indicate that 87% of patients presented quality of life improvements after at-home tooth bleaching, which confirms the existence of a strong relationship of self-esteem and self-perception with dental esthetic improvement.

At-home bleaching has been a great ally in dental esthetics for some time and, although it involves certain costs, risks, and disadvantages (RAO, et al., 2009) (ANAGNOUSTOU, et al., 2010) (BERGER, et al., 2008), one of the greatest reasons of the popularity of this treatment is the conceived idea that oral health is intimately related

to the white color of teeth, as well as the current accessibility to such a procedure (TEIXEIRA, 2013).

As for the high patient satisfaction level of this study, the present meta-analysis corroborates other studies that show good efficacy of at-home bleaching on the tooth color of the volunteers (CARLOS et al., 2017) (MATIS et al., 2002) (GOMES et al., 2009), highlighting this potential relationship between tooth color improvement and patient satisfaction.

Considering that the face is the most notorious third, it becomes the prevalent physical characteristic related to the development of self-esteem, promoting better social interactions, self-confidence, and improved relationships (BOS A., HOOGSTRATEN J., PRAHL-ANDERSEN B., 2003). Even small differences in dental esthetics may have a significant effect on the quality of life (KLAGES U., BRUCKNER A., ZENTNER A., 2004), affecting the psychological and emotional state of individuals (KHAN M., FIDA M., 2008). Therefore, individuals satisfied with their physical appearance tend to be more extroverted and accomplished in social interactions (KLAGES U. et al., 2006).

Moreover, the current concept of health and disease may be considered biopsychosocial, implying that diseases have a multifactorial nature focusing on psychological issues in this process (MONCADA L. et al., 2009). Thus, explanations, causes, and even the possibility of a cure would involve biological and psychosocial aspects, promoting each person to a unit and their participation in the recovery process (MONCADA L. et al., 2009), creating the concept of health-related quality of life (NÚÑEZ L. et al., 2013).

However, several studies assessing the bleaching effect on teeth also analyzed sensitivity and the involvement of patients with the treatment (GEUS et al., 2018) (MEIRELES et al., 2014), considering that it is performed at home by the patient. Hence, high sensitivity indices may reduce satisfaction or even cause treatment withdrawal. Therefore, several questions should be considered regarding the low patient satisfaction rates.

Randomized clinical trials were selected as an inclusion criterion because when well executed and designed, they present a high quality of scientific evidence and are considered the gold standard for the efficacy of interventions (MILLS et al., 2009). Moreover, parallel studies, which represent more than 90% of the studies selected in this

systematic review, are considered the gold standard of clinical trials because they are not susceptible to the effects of previous treatments (CLEOPHAS & VOGEL, 1998).

There were nine different assessment questionnaires used in the studies, with specific ones such as the OHIP and Rosenberg self-esteem scale and broader ones such as forms and spontaneous response. Thus, the result should be analyzed with caution due to the lack of standardization and, consequently, the difficulty of grouping the studies for a more precise assessment.

Additionally, it is worth noting the need for further studies grouping the same assessment questionnaires to reinforce the evidence that at-home tooth bleaching improves the quality of life of patients.

Conclusion

This systematic review with meta-analysis allows concluding that there is an improvement in the quality of life of patients subjected to at-home tooth bleaching. However, further studies are required to group the same questionnaires used for assessment.

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APPENDIX

PROJECT REGISTRATION IN THE INTERNATIONAL PROSPECTIVE REGISTER OF SYSTEMATIC REVIEWS (PROSPERO).

preferred format includes details of both inclusion and exclusion criteria.

At home tooth bleaching.

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

At home tooth bleaching.

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Inclusion criteria: randomized controlled trials that evaluted the quality of life of patients submitted to dental bleaching. We will include only parallel, split-mouth clinical trials in humans.

Exclusion criteria: non-controlled clinical trials, editorial letters, case reports and case series will be excluded.

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or exclusion criteria.

Inclusion criteria: patients with discolored teeth.

Exclusion criteria: patients not eligible for cosmetic treatments due to the presence of other important pathological conditions such as dental caries, need for endodontics, orthodontics and periodontal treatment.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

Quality of life assessment (assessed with different questionnaires, e.g: OHIP- 14, PIDAC, OES, among others, as noted in the studies).

* Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

The effects will be evaluated after the end of treatment (mean difference or standardized mean difference or risk ratio).

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

No restrictions will be placed on the publication date or languages, and all relevant studies will be translated and reviewed. We will search the abstracts of the annual conference of the International Association for Dental Research (IADR) and their regional divisions (2001-2019).

We are also going to explore the grey literature using the database System for Information on Grey literature in Europe (SIGLE), and dissertations and theses using the ProQuest Dissertations and Theses Fulltext database, and Periódicos Capes Theses database as well.

To locate unpublished and ongoing trials related to the review question, we will search the following clinical trials registries: Current Controlled Trials (www.controlledtrials.com), International Clinical trials registry plataforma (http://apps.who.int/trialsearch/), The ClinicalTrials.gov (www.ClinicalTrials.gov), Rebec (www.rebec.gov.br), EU Clinical Trials Register (https://www.clinicaltrialsregister.eu).

The search strategy will be appropriately modified for each database and executed by two reviewers to identify eligible studies. The full text versions of the papers that appear to meet the inclusion criteria will be retrieved for further assessment and data extraction.

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible. Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Improve in quality of life.

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Inclusion criteria: Patients with permanent dentition with discolored teeth.

Exclusion criteria: patients not eligible for cosmetic treatments due to the presence of other important pathological conditions such as dental caries, need for endodontics, orthodontics and periodontal treatment.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The

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11. * Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country now MUST be entered for each person, unless you are amending a published record.**

Mrs ANNA ROMBALDO. UNIOESTE
Dr Fabiana Scarparo Naufel. UNIVERSIDADE ESTADUAL DO OESTE DO PARANÁ
Dr Bianca Medeiros Maran. UNIVERSIDADE ESTADUAL DO OESTE DO PARANÁ
Maria Daniela Basso de Souza. UNIVERSIDADE ESTADUAL DO OESTE DO PARANÁ

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

None

Grant number(s)

State the funder, grant or award number and the date of award

None

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

Does at-home dental bleaching really improve the quality of life of patients with tooth discoloration?

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

To identify trial investigations that must be included for this review, we shall search on the electronic databases MEDLINE via PubMeb, Scopus, Web of Science, Latin American and Caribbean Health Sciences Literature database (LILACS), Brazilian Library in Dentistry (BBO) and Cochrane Library.

We will also hand-search the reference lists of all primary studies for additional relevant publications and the related articles link of each primary study in the PubMed database without restrictions to publication date or languages.

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Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

ANNA CAROLINA CENCI MATICK ROMBALDO

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Mrs.ROMBALDO

7. * Named contact email.

Give the electronic email address of the named contact.

annamatick@gmail.com

8. Named contact address

Give the full institutional/organisational postal address for the named contact.

RUA NATAL 2591, APTO 402, CEP 85807-100

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

(44) 99905-9955

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

UNIVERSIDADE ESTADUAL DO OESTE DO PARANÁ

Organisation web address:

anna.matick@unioeste.br

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UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

*Fields that have an **asterisk (*)** next to them means that they **must be answered.** **Word limits** are provided for each section. You will be unable to submit the form if the word limits are exceeded for any section. Registrant means the person filling out the form.*

1. * Review title.

Give the title of the review in English

Patients with dental discoloration submitted to at-home dental bleaching can you improve the quality of life?

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

Pacientes com descoloração dental submetidos ao clareamento dental caseiro podem ter melhora na qualidade de vida?

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

28/09/2020

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

31/08/2021

5. * Stage of review at time of this submission.

Tick the boxes to show which review tasks have been started and which have been completed. Update this field each time any amendments are made to a published record.

Reviews that have started data extraction (at the time of initial submission) are not eligible for inclusion in PROSPERO. If there is later evidence that incorrect status and/or completion date has been supplied, the published PROSPERO record will be marked as retracted.

This field uses answers to initial screening questions. It cannot be edited until after registration.

The review has not yet started: No

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Please provide anticipated publication date

Review_Ongoing

39. Any additional information.

Provide any other information relevant to the registration of this review.

40. Details of final report/publication(s) or preprints if available.

Leave empty until publication details are available OR you have a link to a preprint. List authors, title and journal details preferably in Vancouver format.

Give the link to the published review or preprint.

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Select each language individually to add it to the list below, use the bin icon to remove any added in error.
English

There is an English language summary.

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved.

Brazil

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

Add web link to the published protocol.

Or, upload your published protocol here in pdf format. Note that the upload will be publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

Give brief details of plans for communicating review findings.?

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

Quality of life, Tooth bleaching, Tooth discoloration

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

38. * Current review status.

Update review status when the review is completed and when it is published.New registrations must be ongoing.

Musculoskeletal
No

Neurological
No

Nursing
No

Obstetrics and gynaecology
No

Oral health
Yes

Palliative care
No

Perioperative care
No

Physiotherapy
No

Pregnancy and childbirth
No

Public health (including social determinants of health)
No

Rehabilitation
No

Respiratory disorders
No

Service delivery
No

Skin disorders
No

Social care
Yes

Surgery
No

Tropical Medicine
No

Urological
No

Wounds, injuries and accidents
No

Violence and abuse
No

31. Language.

Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system
No

Cancer
No

Cardiovascular
No

Care of the elderly
No

Child health
No

Complementary therapies
No

COVID-19
No

Crime and justice
No

Dental
Yes

Digestive system
No

Ear, nose and throat
No

Education
No

Endocrine and metabolic disorders
No

Eye disorders
No

General interest
No

Genetics
No

Health inequalities/health equity
No

Infections and infestations
No

International development
No

Mental health and behavioural conditions
No

participant will be included in each group or covariate investigated. State the planned analytic approach.
The subgroup analysis will be conducted for different questionnaires assessed in relation to quality of life.

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Cost effectiveness
No

Diagnostic
No

Epidemiologic
No

Individual patient data (IPD) meta-analysis
No

Intervention
No

Meta-analysis
No

Methodology
No

Narrative synthesis
No

Network meta-analysis
No

Pre-clinical
No

Prevention
No

Prognostic
No

Prospective meta-analysis (PMA)
No

Review of reviews
No

Service delivery
No

Synthesis of qualitative studies
No

Systematic review
Yes

Other
No

None

* Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

None

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Articles will be selected by title and abstracts according to the previously described search strategy. Duplicated articles published in more than one database will be considered only once. Full-text articles will also be obtained when the title and abstract have sufficient information to make a clear decision. Subsequently, two reviewers will classify those which met the inclusion criteria. To handle with such a large number of studies, we will use a study ID for each eligible study, combining first author and year of publication. Any disagreements between the reviewers over the eligibility of particular studies will be resolved through discussion with a third reviewer.

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

The assessment criteria six items: selection bias (adequate sequence generation and allocation concealment), performance bias (patient and operator blinding), detection bias (evaluator blinding), attrition bias (incomplete outcome data), reporting bias (selective outcome reporting), and other bias. Any other type of bias identified during the review will also be recorded and considered, and if needed, by consulting a fourth reviewer.

Each domain level will judged as having low, high, or unclearrisk o bias. At the study level, the study will at low risk of bias if all five domains of the risk of bias tool will at low risk of bias. If one or more domains will judged to have an unclear risk, the study will judged as an unclear risk; if at least one item will at high risk of bias, the study will considered to have a high risk of bias.

28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data. If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

Data will analyzed using the software RStudio statistical program (Version1.3.1093 2009-2020 RStudio, PBC). Meta-analyses were performed in all eligible studies

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or