DIODE LASER AS AN ADJUNCTIVE TREATMENT FOR PERI-IMPLANT MUCOSITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Diode laser as an adjunctive treatment for peri-implant mucositis: a systematic review and meta-analysis

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Background: The early detection and treatment of peri-implant mucositis may help in reducing inflammatory parameters and arrest disease progression to peri-implantitis. The potential clinical benefits of using different adjunctive therapies, such as the diode laser, are still not clear.

Aim: The aim of this systematic review and meta-analyses was to evaluate the outcomes of using diode laser on the treatment of peri-implant mucositis in terms of changes in periodontal parameters.

Materials and Methods: Electronic databases were searched to identify randomized controlled trials (RCTs) that compared the combined use of mechanical debridement and diode laser with mechanical debridement alone. The risk of bias was assessed using the Cochrane Collaboration's Risk of Bias tool. Data were analyzed using a statistical software program.

Results: A total of 149 studies were identified, of which, three RCTs with 311 dental implants in 311 participants were included. Overall meta-analysis showed more reduction in probing pocket depths (mean difference (MD) -0.36; 95% confidence interval (CI) -0.88 to 0.16; P = 0.18) and bleeding on probing (MD -0.71; 95% CI -1.58 to 0.16; P = 0.11) at three months in favour of diode laser, but the differences were not statistically significant.

Conclusion: In the management of peri-implant mucositis, the combined use of diode laser and mechanical debridement have positive short-term effect on periodontal parameters but any additional clinical advantage over mechanical debridement alone is still not clear. Long-term, well-designed RCTs are still needed to substantiate the clinical benefits of using diode laser as an adjunctive therapy in the management of peri-implant mucositis.

DEDICATION

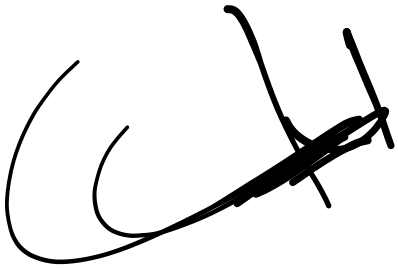
To my family, and special thanks to my kids (Khalid and Zayed) for their constant encouragement throughout this journey.

DECLARATION

I declare that all the content of this thesis is my own work. There is no conflict of interest with any other entity or organization

Name: Israa Amir Fadhel

Signature:



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1. INTRODUCTION

The long-term success and predictability of the dental implant therapy across various prosthodontic indications is well established (Buser et al., 2017). However, implant failure and peri-implant diseases (i.e., peri-implant mucositis and peri-implantitis) occur in a significant proportion of patients (Atieh et al., 2021, Atieh et al., 2013, Atieh et al., 2019, Atieh et al., 2020, Berryman et al., 2020, Tawse-Smith et al., 2015).

Peri-implant diseases are diagnosed based on the routine monitoring of dental implants using clinical and radiographical parameters. Mucosal condition, plaque assessment, peri-implant probing depth, peri-implant sulcular fluid analysis, suppuration, peri-implant keratinized tissue width, implant mobility, discomfort, resonance frequency analysis, and radiographs are some of the parameters that can be used to assess the presence of peri-implant disease and the its severity (Salvi and Lang, 2004). Several definitions were previously described in the literature to define peri-implant diseases. In 2011, (Heitz-Mayfield et al.) described the condition as peri-implant mucositis when the criteria of bleeding on probing and no bone loss are present. Moreover, (Porras et al., 2002) determined bleeding on probing, using the modified bleeding index as evidence of inflammation, plaque, and probing pocket depth ≤5 mm to be the diagnostic criteria for peri-implant mucositis. Whereas, (Felo et al., 1997) stipulated the presence of probing pocket depth ≤3 mm in his defined cases in addition to the presence of bleeding on probing and plaque. This lack of consistency in the case definition between the studies makes it difficult for researchers to investigate the natural history, pathophysiology, etiology and treatment of the peri-implant disease and conditions, as well as the clinician to appropriately diagnose and treat patients. Therefore, a classification scheme was finally introduced to overcome the heterogenous case definitions throughout the literature (Caton et al., 2018).

Peri-implant mucositis is therefore defined as a reversible plaque-induced inflammatory disease of the peri-implant soft tissues surrounding a functioning ossoeintegrated dental implant. Its diagnosis is based on clinical signs of inflammation without any radiographical marginal bone loss. Peri-implantitis, on the other hand, is a plaque-induced inflammatory diseases of both the soft and hard tissues surrounding a functioning osseointegrated dental implant. Beside the clinical signs of inflammation, radiographic marginal bone loss beyond initial bone remodeling is present (Berglundh et al., 2018). Depending on case definitions and threshold of marginal bone loss, it has been estimated that peri-implant mucositis can occur in 63.4% of patients and 30.7% of implants, while peri-implantitis can occur in 18.8% and 9.6% of patients and implants, respectively (Atieh et al., 2013).

Accumulation of pathogenic bacteria and the formation of biofilms around dental implants play a key role in the initiation of peri-implant mucositis that could progress to peri-implantitis if left untreated (Jepsen et al., 2015, Salvi and Zitzmann, 2014). The main aim of peri-implant disease treatment, particularly peri-implant mucositis, is removing the biofilm surrounding the implant without changing or jeopardizing implant surface characteristics, with the goal to establish a healthy peri-implant tissue (Figuero et al., 2014). Hence, the prevention of its progression to an irreversible and often challenging to treat peri-implantitis (Salvi and Zitzmann, 2014). The effectiveness of oral home care measures and non-surgical treatment approaches in the management of peri-implant mucositis can improve the clinical signs of inflammation. However, complete resolution may not always be achievable due to the complexity of implant designs and surface characteristics impeding effective removal of the biofilm (Schwarz et al., 2015). The use of adjunctive therapies, such as topical antiseptics (Porras et al., 2002, Felo et al., 1997), local and systemic antimicrobials (Suarez-Lopez

Del Amo et al., 2016), air-abrasive devices (Riben-Grundstrom et al., 2015) and lasers (Albaker et al., 2018), have been suggested to improve the efficacy of conventional mechanical debridement. The benefits of such additional therapies, however, remains unclear.

2. REVIEW OF THE LITERATURE

The term "laser" stands for "light amplification by stimulated emission of radiation," and it was first used in periodontics in the 1990s as a diagnostic, surgical, and physiologic technique (Midda, 1992). There are several types of lasers that has been identified in implant therapy, such as diode laser (Mizutani et al., 2016).

Dental diode lasers are FDA approved. They have wavelengths that extend from visible to near infrared, with a range from 800 to 980 nm. An optical flexible quartz fiber of 200 to 600 μm is used to deliver a laser beam. The dental power output ranges from 2 to 10 watts and can be used in either continuous or pulsed mode. The high absorption in melanin and hemoglobin allow diode lasers to coagulate, cut, bleach and disinfect with minimal damage to hard tissues and better postoperative healing (AAP, 2002, Goharkhay et al., 1999). The advantages of diode laser in allowing precise cuts, controlling hemostasis, and minimal postoperative pain or swelling have been demonstrated in a variety of soft tissue surgeries (Verma et al., 2012, Hilgers and Tracey, 2004, Kamma et al., 2009).

The use of diode laser has been described as one adjunctive aid in the treatment of peri-implant mucositis (Heitz-Mayfield and Mombelli, 2014). Diode laser, in peri-implant conditions, could offer additional clinical benefits in terms of inactivating pigmented gram-negative anaerobic bacterial rods (Chan and Lai, 2003) and disinfecting rough and irregular implant surfaces that are difficult to reach via conventional mechanical debridement. In addition, diode laser may decontaminate implant surfaces with minimal damage to implants (Romanos et al., 2000). However, a recent study with a 12 months follow up, showed a minimal additional benefit of the adjunct use of diode laser in the treatment of peri-implant mucositis (Mariani et al., 2020).

Several narrative and systematic reviews have evaluated the effects of different types of lasers in the treatment of peri-implantitis (Ashnagar et al., 2014, Mattar et al., 2021, Ramanauskaite et al., 2016, Ting et al., 2018). However, the evidence is still emerging and the true impacts of the adjunctive use of diode laser in the treatment of peri-implant mucositis remain to be objectively assessed.

3. AIM

The aim of this systematic review and meta-analyses, therefore, was to evaluate the outcomes of treatment of peri-implant mucositis using diode laser in terms of changes in periodontal parameters based on the available evidence from randomized controlled trials (RCTs).

4. MATERIALS AND METHODS

The present systematic review was prepared in accordance with the guidelines of the Cochrane Collaboration (Higgins et al., 2022) and the statement of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (Page et al., 2021). A well-defined question of participant, intervention, comparison, outcome (PICO) (Higgins et al., 2019, Richardson et al., 1995) was formulated:

Participant: Human adults aged ≥ 18 years that require treatment of peri-implant mucositis.

Intervention: Mechanical debridement and diode laser (810 nm and 980 nm).

Comparison: Mechanical debridement alone.

Outcomes: Changes in probing pocket depths, bleeding on probing, plaque score and peri-implant mucosal recession.

The study has been registered at the National Institute for Health Research (NHR) under the PROSPERO ID CRD42022306877. Ethical approval was not required for this systematic review.

4.1 Types of studies

4.1.1 Inclusion criteria

This review included RCTs comparing combined use of mechanical debridement and diode laser to mechanical debridement alone in the treatment of peri-implant mucositis. The included studies must report on clinical parameters including probing pocket depths, bleeding on probing, plaque score or peri-implant mucosal recession. No language restrictions or publication status were employed.

4.1.2 Exclusion criteria

Non-RCTs, retrospective studies, case series, case reports, histomorphometric research, and studies that did not provide sufficient data were excluded.

4.2 Type of participants

Participants that were 18 years of age or older and require treatment of peri-implant mucositis.

4.3 Types of interventions

Comparing combined use of mechanical debridement and diode laser (810 nm and 980 nm) to mechanical debridement alone in the treatment of peri-implant mucositis.

4.4 Outcome measures

4.4.1 Primary outcomes:

Changes in probing pocket depths.

4.4.2 Secondary outcomes :

Changes in bleeding on probing.

Changes in plaque score.

Changes in peri-implant mucosal recession.

4.5 Search Strategy

The search protocol followed standard procedures (Faggion et al., 2013, Higgins et al., 2019). The following electronic databases were searched for ongoing and unpublished trials up to November 11 2021: MEDLINE, EMBASE, The Cochrane Central Register of Controlled Trials (CENTRAL), MetaRegister, ClinicalTrials.gov, and the System for Information on Grey Literature in Europe (http://www.opengrey.eu) (Table 1). The search was performed independently and in duplicate by two authors (M.A. and I.F.).

Manual search of the last five years of relevant dental journals (*Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *Implant Dentistry*, *International Journal of Oral and Maxillofacial Implants*, *International Journal of Periodontics and Restorative Dentistry*, *Journal of Clinical Periodontology*, *Journal of Periodontology* and *Lasers in Medical Science*) and bibliographies of all eligible papers was carried out to look for other additional studies.

Table 1 Databases and search terms

Databases	**Keywords**
Published studies PubMed (1965 - November 11, 2021)	(peri-implant mucositis OR periimplant mucositis OR peri-implant disease* OR periimplant disease*) AND (non-surgical treatment OR nonsurgical treatment OR diode laser)
EMBASE via Ovid (1947 - November 11, 2021)	(peri-implant adj mucositis).mp OR (periimplant adj mucositis).mp. OR (peri-implant adj disease$).mp. OR (periimplant adj disease$).mp. AND (non-surgical adj treatment).mp. OR (nonsurgical adj treatment).mp. OR (diode adj laser).mp.

Cochrane Central Register of Controlled Trials (CENTRAL) via Ovid (November 11, 2021)	(peri-implant adj mucositis).mp OR (periimplant adj mucositis).mp. OR (peri-implant adj disease$).mp. OR (periimplant adj disease$).mp. AND (non-surgical adj treatment).mp. OR (nonsurgical adj treatment).mp. OR (diode adj laser).mp.
Unpublished studies MetaRegister of controlled trials OpenGrey (www.opengrey.eu) ClinicalTrials.gov (November 11, 2021)	(peri-implant mucositis OR periimplant mucositis OR peri-implant diseases OR periimplant diseases) AND (non-surgical treatment OR nonsurgical treatment OR diode laser)

4.6 Selection of studies

Two reviewers (M.A. and I.F.) independently and in duplicate examined the retrieved citations on the basis of title, abstract, and keywords. Irrelevant papers were excluded and full-texts of the remaining ones were obtained. An eligibility form was used to examine papers for inclusion in the review. Any disagreements were resolved by discussion to reach a consensus. In the event of duplicate papers, the one with the most relevant and sufficient information was selected. All the reasons for exclusion were reported.

4.7 Data collection

Two authors (M.A. and I.F.) used a data extraction form and independently collected the following information from the included studies: 1) Study characteristics: title, authors' names, contact address, study location, language of publication, year of publication, published or unpublished data, source of study funding, study design (parallel group or split mouth), method of randomization, allocation concealment and blinding (participants, investigators, outcome examiners). 2) Participants: demographic characteristics, inclusion/exclusion criteria, number of participants in test and control groups, number of withdrawals and reasons for dropouts. 3) Interventions: number of participants where treatment of peri-implant mucositis was performed using mechanical debridement and diode laser. 4) Comparison: number of participants where treatment of peri-implant mucositis was performed using mechanical debridement alone. 5) Outcomes: changes in probing pocket depths, bleeding on probing, plaque score and peri-implant mucosal recession. 6) Length of the observation period. Any disagreements between reviewers were resolved by discussion to reach a consensus. Corresponding authors of the included studies were contacted for additional information if required.

4.8 Quality assessment of included studies

Two reviewers (M.A. and I.F.) used the Cochrane Collaboration's Risk of Bias (RoB) tool for randomized studies of interventions to independently assess the included human studies to determine the risk of bias (Higgins et al., 2019). The RoB tool for RCTs consists of seven domains (sequence generation, allocation concealment, blinding of participants and investigators, blinding of outcome assessment, incomplete data outcome, selective outcome reporting, and potential sources of bias). The first part of the tool describes each domain while the second part categorizes studies into those

having (i) low risk of bias if all the criteria were met, (ii) unclear risk of bias if one or more criteria were partially met, or (iii) high risk of bias if one or more criteria were not met.

4.9 Data synthesis

A statistical software program (Review Manager (RevMan) software, version 5.3, The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark) was used to conduct meta-analyses for studies of similar comparisons reporting the same outcome measures. For example: continuous data, such as changes in probing pocket depths, were expressed in mean difference (MD) or standardized mean difference (SMD) and 95% confidence intervals (CIs). Dichotomous data were expressed as risk ratio (RR) estimates and 95% CIs. Random-effects model was used to pool the results from more than one study as heterogeneity between studies was expected. Split-mouth and parallel group studies were combined using the generic inverse variance option in the statistical software program.

With fewer than 10 studies, publication bias was not formally assessed because the power to detect publication bias was limited (Higgins et al., 2019). The statistical heterogeneity across different studies was assessed by means of the Cochran's test for heterogeneity and I^2 statistic (Higgins et al., 2019). An I^2 value of > 50 indicated a substantial heterogeneity. The unit of analysis was the implant rather than the participant as the outcomes may have varied between the two treatment modalities.

5. RESULTS

5.1 Characteristics of the study settings

A total of 149 studies were retrieved from the databases (Figure 1). After titles and abstracts were examined independently and in duplicate by two review authors (M.A. and I.F.), five studies were eligible for full-text review (Aimetti et al., 2019, Lerario et al., 2016, Mariani et al., 2020, Sanchez-Martos et al., 2020a, Tenore et al., 2020). Two studies (Lerario et al., 2016, Mariani et al., 2020) were subsequently excluded and as a result three studies (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020) were included in the present review (Table 2). Of the three included studies, two were conducted in the Italy (Aimetti et al., 2019, Tenore et al., 2020), and one in Spain (Sanchez-Martos et al., 2020a). All the included RCTs were parallel-group and self-funded studies which took place in university setting.

Figure 1 Flowchart of the search process

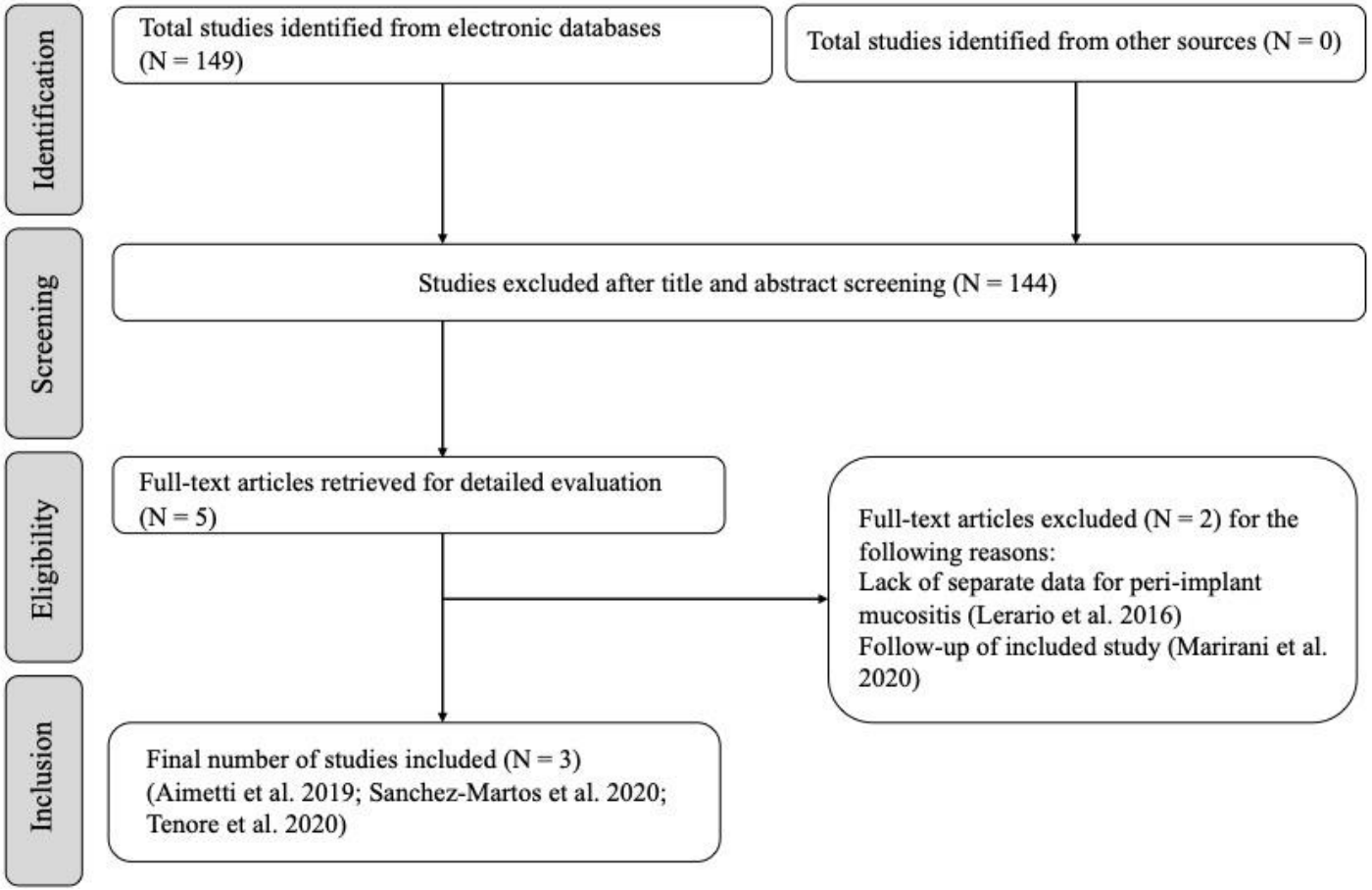


Table 2 Characteristics of the included studies

	Aimetti et al. 2019	**Sanchez-Martos et al. 2020**	**Tenore et al. 2020**
Study design	RCT (parallel group)	RCT (parallel group)	RCT (parallel group)
Location	University of Turin, Turin, Italy	European University of Valencia, Valencia, Spain	University of Rome, Rome, Italy
Number evaluated (participants/implants) DL MD	220/220 110/110 110/110	68/68 34/34 34/34	23/23 11/11 12/12

Age (years)	57.5 ± 10.1 (range 32-78)	57.0 ± 11.39	56.1 (range 20-80)
Smokers n (%) DL MD	 14 (12.73) 20 (18.18)	 2 (5.88) 6 (17.65)	 0 (0) 0 (0)
History of periodontitis n (%) DL MD	 54 (49) 45 (41)	 NR NR	 NR NR
Implant surface characteristics n (%) Minimally rough (machined) < 1.0 µm DL	 NR	 0	 NR

MD Moderately rough 1.0-1.9 µm	NR	0	NR
DL	NR	34	NR
MD Rough ≥ 2.0 µm	NR	34	NR
DL	NR	0	NR
MD	NR	0	NR
Implant time in function (years)			
DL	6.8 ± 3.6	3.1 ± 1.5	NR
MD	7.4 ± 4.4	3.1 ± 1.5	NR

Implant location Incisors n (%)			
DL	8	NR	NR
MD	12	NR	NR
Canines n (%)			
DL	6	NR	NR
MD	9	NR	NR
Premolars n (%)			
DL	52	NR	NR
MD	42	NR	NR
Molars n (%)			

DL MD	44 47	NR NR	NR NR
Mechanical debridement	Ultrasonic and manual instruments (titanium-coated curettes or carbon fiber curettes)	Ultrasonic and manual instruments (plastic curettes)	Ultrasonic and manual instruments (titanium-coated or carbon fiber curettes)
Laser settings	980 nm 2.5 watt 10 KHz pw, 30 seconds	810 nm[*] 1 watt in pulsed mode 30 seconds	980 nm[†] 1 watt in pulsed mode 60 seconds
Methods of assessment	Periodontal probe	Periodontal probe[‡]	Periodontal probe[§]

Changes in PPDs implant (mm) at three months DL MD	 -0.6 ± 0.8 -0.4 ± 0.7	 -0.21 ± 0.06 -0.14 ± 0.08	 -1.06 ± 0.11 -0.26 ± 0.15
Changes in number of implant sites with BoP at three months DL MD	 NR[I] NR[I]	 -0.91 ± 0.80 -0.61 ± 0.13	 -3.45 ± 0.20 -2.00 ± 0.22
Changes in number of implant sites with plaque at three months DL	 NR[I]	 -0.34 ± 0.11	 NR

MD	NR[I]	-0.17 ± 0.09	NR
Mucosal recessions of 1-3 mm at three months n (%) DL MD	 6 (5.45) 9 (8.18)	 NR NR	 NR NR
Follow-up period (months)	3	3	3

RCT: randomized controlled trial; DL: diode laser; MD: mechanical debridement; PPD: probing pocket depth; BoP: bleeding on probing; NR: not reported
[*]Fox® diode laser, A.R.C. Laser GmbH, Nurnberg, Germany
[†]Raffaello®, Dental Medical Technologies, Lissone, Italy
[‡]North Carolina Probe, Hu-Friedy, Leinmen, Germany
[§]Goldman-Fox William, Asa Dental S.P.A., Italy
[I]Not reported in terms of number of sites

5.2 Characteristics of participants at baseline

5.2.1 Inclusion criteria

1. Aged > 18 (Sanchez-Martos et al., 2020a), or 20 to 80 years (Tenore et al., 2020).
2. Healthy periodontium (Aimetti et al., 2019, Sanchez-Martos et al., 2020a) or history of treated periodontitis without residual probing pocket depths of ≥ 5 mm (Aimetti et al., 2019).
3. Full mouth plaque score of ≤ 20% (Aimetti et al., 2019).
4. Full mouth bleeding score of ≤ 20% (Aimetti et al., 2019).
5. Presence of at least one implant site with bleeding on probing and probing pocket depth of ≥ 4 mm (Aimetti et al., 2019, Sanchez-Martos et al., 2020a) and ≤ 6 mm) (Tenore et al., 2020).
6. Absence of radiographic marginal bone loss beyond the initial bone remodeling (Aimetti et al., 2019, Sanchez-Martos et al., 2020a).
7. Absence of occlusal overload (Aimetti et al., 2019).
8. Lack of any detected cement remnants (Aimetti et al., 2019).
9. At least six months of functional loading prior to enrollment in the study (Aimetti et al., 2019).
10. Non-smokers or light smokers (<10 cigarettes/day) (Aimetti et al., 2019).

5.2.2 Exclusion criteria

1. Systemic conditions and/or medications that may affect the treatment outcomes (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020).
2. Use of antibiotics within six months prior to initial assessment (Sanchez-Martos et al., 2020a).
3. Long-term use of anti-inflammatory drugs (Sanchez-Martos et al., 2020a).

4. History of head and neck radiotherapy (Sanchez-Martos et al., 2020a).
5. Pregnancy or lactation (Aimetti et al., 2019).
6. Presence of peri-implantitis (Aimetti et al., 2019, Tenore et al., 2020).
7. Previous non-surgical peri-implant treatment within six months or surgical peri-implant treatment within 12 months prior to initial assessment (Sanchez-Martos et al., 2020a).
8. Presence of cement-retained or multiple implant-supported prostheses (Sanchez-Martos et al., 2020a).
9. Smoking (Tenore et al., 2020).

5.3 Case definitions

Two studies (Aimetti et al., 2019, Sanchez-Martos et al., 2020a) defined peri-implant mucositis as the presence of probing pocket depth of ≥ 4 mm with bleeding and/or suppuration on probing, and absence of any radiographic bone loss beyond marginal bone level changes resulting from initial bone remodeling, marginal bone loss of ≤ 1 mm as compared with baseline radiographs or marginal bone loss of < 2 mm in the absence of previous examination (Sanz et al., 2012, AAP, 2013). In addition, one study (Tenore et al., 2020) required the presence of probing pocket depth of ≤ 6 mm with bleeding and/or suppuration on probing for the diagnosis of peri-implant mucositis.

5.4 Characteristics of the interventions

The combined mechanical debridement and diode laser group included the use of 980-nm diode laser at 2.5 watt (Aimetti et al., 2019), 980-nm diode laser at 1.0 watt (Tenore et al., 2020), or 810-nm diode laser at 1.0 watt (Sanchez-Martos et al., 2020a) in pulsed mode. A 300-µm optical fiber was inserted parallel to the long axis of the implant and moved in apico-coronal and mesio-distal directions for 30 (Aimetti et al., 2019, Sanchez-Martos et al., 2020a) or 60 seconds (Tenore et al., 2020). Each diode laser

application was preceded and followed by pocket irrigation with 3% hydrogen peroxide solution for 10 seconds (Aimetti et al., 2019). Another study (Sanchez-Martos et al., 2020a) used 0.12% chlorhexidine and 0.05% cetylpyridinium chloride for pocket irrigation while the remaining one (Tenore et al., 2020) applied 1% chlorhexidine gel in the peri-implant pockets. Mechanical debridement was then carried out using ultrasonic and manual instruments such as titanium coated Gracey (Aimetti et al., 2019, Tenore et al., 2020), carbon fiber (Aimetti et al., 2019, Tenore et al., 2020) or plastic curettes (Sanchez-Martos et al., 2020a). Both diode laser application and mechanical debridement were repeated three times in one study (Aimetti et al., 2019).

In the mechanical debridement group, only instrumentation with ultrasonic and manual curettes were used (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020) with an operating time ranging between 7 and 10 minutes (Aimetti et al., 2019). In both groups, prosthetic supra-structures were removed in one study (Sanchez-Martos et al., 2020a) prior to mechanical debridement. At one- and three-month recalls, participants received reinforcement in oral home care (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020) and professional implant cleaning with rubber cups and polishing paste (Aimetti et al., 2019).

5.5 Characteristics of outcome measures

5.5.1 Primary outcome measures

- Changes in probing pocket depths as measured by periodontal probe (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020).

5.5.2 Secondary outcome measures

- Changes in bleeding on probing as measured by periodontal probe (Sanchez-Martos et al., 2020a, Tenore et al., 2020).

- Changes in plaque score as measured by periodontal probe (Sanchez-Martos et al., 2020a).
- Changes in peri-implant mucosal recession as measured by periodontal probe (Aimetti et al., 2019).

5.6 Risk of bias

Methods of randomization and allocation concealment were adequately described in all studies and hence were all judged to be at low risk of bias for those domains (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020). One study (Aimetti et al., 2019) reported on blinding the outcome assessors and was judged to be at low risk of bias while the remaining two studies did not mask the data assessors and were judged to be at high risk of bias (Sanchez-Martos et al., 2020a, Tenore et al., 2020). For attrition and reporting biases, all the studies (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020) were rated as low (Figure 2, Table 3).

Figure 2: Assessment of applicability concerns and risk of bias of the included studies presented with low (green), unclear (yellow) and high (red) risk of bias

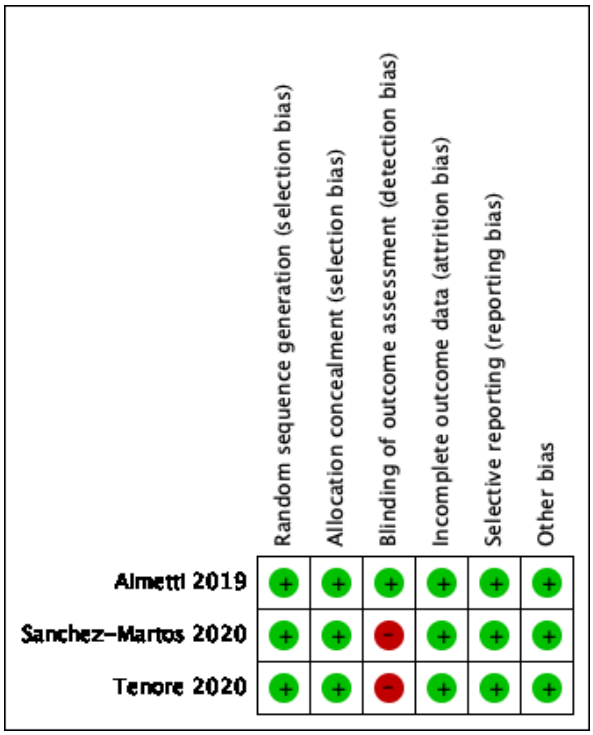


Table 3 Assessment of risk of bias of the included studies

	Aimetti et al. 2019	**Sanchez-Martos et al. 2020**	**Tenore et al. 2020**
Random sequence generation (selection bias)	Low risk *Reported in the article "A balanced randomly permuted block was used to prepare the randomization table"*	Low risk *Reported in the article "using a randomized system based on stratified blocks"*	Low risk *Reported in the article "patients were randomly allocated from a computer-generated list of random numbers*"
Allocation concealment (selection bias)	Low risk *Reported in the article "To conceal assignment, forms with the treatment modality were put into identical and opaque envelopes"*	Low risk *Reported in the article "The allocation concealment was carried out through the use of sealed opaque envelopes"*	Low risk *Reported in the article "Allocation concealment was achieved through the provision, by professionals not involved in patient enrolment, of a numbered sequence of opaque and sealed envelopes"*

Blinding of outcome assessment (detection bias)	Low risk *Reported in the article "Two examiners, who were blinded to the group assignment, performed all measurements of clinical assessment"*	High risk *Reported in the article "The interventions assigned to each group were performed by a calibrated and trained examiner not blind to the group assignment"*	High risk *No information in the article*
Incomplete outcome data (attrition bias)	Low risk *All data presented*	Low risk *All data presented*	Low risk *All data presented*
Selective reporting (reporting bias)	Low risk *All outcomes appear to be detected*	Low risk *All outcomes appear to be detected*	Low risk *All outcomes appear to be detected*
Other bias	None detected	None detected	None detected

5.6.1 Sample size calculation

All studies (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020) reported on the sample size calculation.

5.6.2 Clinical trial registration

No information was provided on whether any of the three studies (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020) was registered before the initiation of the study.

5.7 Effects of interventions

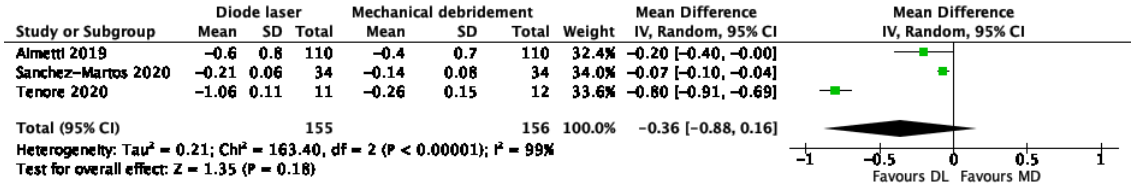
In total, 311 participants with 311 dental implants diagnosed with peri-implant mucositis were included in the present review. Of these, 155 implants were treated using diode laser and mechanical debridement, while the remaining implants were treated with mechanical debridement alone.

5.7.1 Changes in probing pocket depths

All included studies (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020) reported on changes of probing pocket depths. With regard to changes in probing pocket depths at three months, more reduction in probing pocket depths was reported amongst implants treated with mechanical debridement and diode laser compared to those treated with mechanical debridement alone. However, the difference was not statistically significant (MD -0.36; 95% CI -0.88 to 0.16; P = 0.18; Figure 3). Substantial heterogeneity was detected (Chi^2 = 163.40, df = 2 (P < 0.0001); I^2 = 99%).

Figure 3: Comparison: Treatment of peri-implant mucositis: diode laser *versus* mechanical debridement

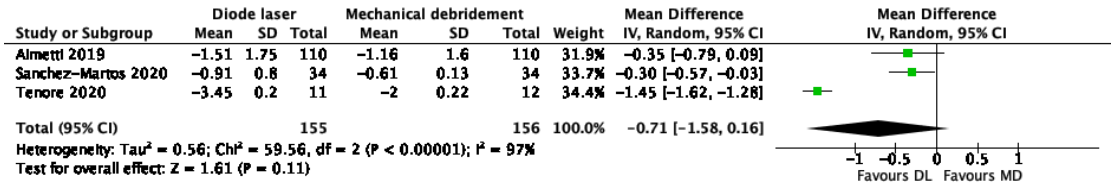
Primary outcomes: changes in probing pocket depths at three months.



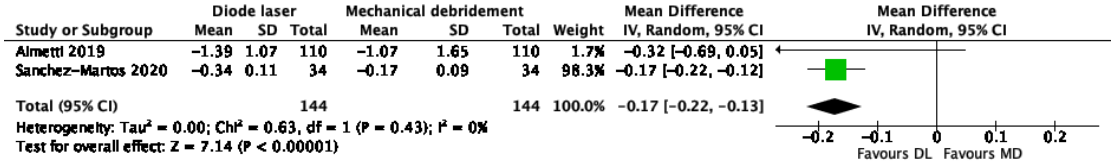
DL: diode laser; MD: mechanical debridement; SD: standard deviation; IV: inverse variance; CI: confidence interval; τ: Kendall tau; z: z test

Figure 4 Comparison: Treatment of peri-implant mucositis: diode laser *versus* mechanical debridement

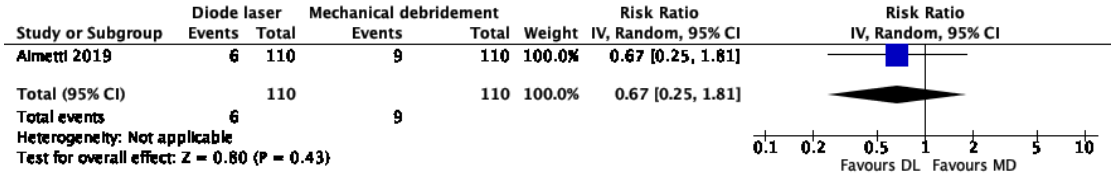
Secondary outcomes: (a) changes in bleeding on probing. (b) changes in plaque score. (c) peri-implant mucosal recession.



(a)



(b)



(c)

DL: diode laser; MD: mechanical debridement; SD: standard deviation; IV: inverse variance; CI: confidence interval; τ: Kendall tau; z: z test

5.7.2 Changes in bleeding on probing and plaque score

All studies (Aimetti et al., 2019, Sanchez-Martos et al., 2020a, Tenore et al., 2020) reported changes in bleeding on probing at three months. The meta-analyses showed that the difference in bleeding on probing was in favour of the combined mechanical debridement and diode laser group, but the difference was not statistically significant (MD -0.71; 95% CI 1.58 to 0.16; P = 0.11; Figure 4a). Significant heterogeneity was detected (Chi^2 = 59.56, df = 2 (P < 0.0001); I^2 = 97%). The changes in plaque score was reported in two studies (Aimetti et al., 2019, Sanchez-Martos et al., 2020a). Significant reduction in plaque score was observed in the diode laser (MD -0.17; 95% CI -0.22 to -0.13; P < 0.0001; Figure 4b) without any substantial heterogeneity (Chi^2 = 0.63, df = 1 (P = 0.43); I^2 = 0%).

5.7.3 Peri-implant mucosal recession

The peri-implant mucosal recession was documented in one study (Aimetti et al., 2019). More sites with 1-3 mm recession were observed amongst implants treated with mechanical debridement compared with the use of diode laser but the difference was not statistically significant (RR 0.67; 95% CI 0.25 to 1.81; P = 0.43; Figure 4c).

6. DISCUSSION

6.1 Summary of main results

The present systematic review compared the clinical outcomes of treatment of peri-implant mucositis with either combined mechanical debridement and diode laser or conventional mechanical debridement alone. Diode laser (810 nm or 980 nm) seems to have positive effects on probing pocket depths, bleeding on probing and peri-implant mucosal levels but without a statistically significant difference to conventional mechanical debridement except for plaque score. Although the decrease in plaque score observed in the diode laser group was statistically significant, its clinical relevance could be considered negligible.

6.2 Quality of evidence

In the present systematic review, we have only included RCTs and followed strict selection criteria in order to minimize the expected heterogeneity and improve the overall quality of our search. Nevertheless, significant heterogeneity amongst the included studies was observed. Sources of heterogeneity could be related to differences in implant designs and surface characteristics as well as the use of different instruments (i.e. ultrasonic with either titanium coated Gracey, carbon fiber or plastic curettes) for mechanically debriding the implant surfaces. Other sources of heterogeneity were the use of different antispetics (i.e. 0.12% chlorhexidine, 0.05% cetylpyridinium chloride and 1% chlorhexidine gel) for pocket irrigation in the test group and the timing of laser application (30 *versus* 60 seconds). However, homogeneity across the included studies was observed in terms of case definitions and observation period. Overall, the generalizability of the findings using diode laser as an adjunctive tool for treatment of peri-implant mucositis is week and it is critical to further assess the effectiveness of diode laser among different implant locations and systems.

While all the included studies described the method of randomization and allocation concealment, two studies (Sanchez-Martos et al., 2020a, Tenore et al., 2020) did not assess the outcomes blindly and were judged to be at high risk of bias. No dropouts were reported, and all of the studies were rated at low risk of attrition and reporting bias. The limitations of absence of assessor blinding and heterogeneity across the studies require cautious interpretation of the outcomes of the present systematic review.

6.3 Applicability of evidence

The early detection and treatment of peri-implant mucositis may allow resolution of peri-implant inflammation and arrest disease progression to peri-implantitis (Pontoriero et al., 1994, Salvi et al., 2012). However, complete resolution is not always achieved (Schwarz et al., 2015) and therefore using an adjunctive therapy may provide additional benefits to conventional mechanical debridement. The present systematic review showed that conventional mechanical debridement with diode laser was effective in reducing inflammatory parameters up to three-month follow-up. However, the peri-implant tissue response to diode laser did not reach statistical or clinical significance in terms of reduction of probing pocket depths, bleeding on probing and plaque score when compared to mechanical debridement alone.

The use of different diode laser settings amongst the included studies might have influenced the efficacy of diode laser as an implant decontamination tool. The frequency and timings of laser application varied between one to three applications and 30 to 60 seconds, respectively. It is assumed that single laser application may not maintain the anti-inflammatory effect (Ramos et al., 2016). Repeating laser application three times in one included study (Aimetti et al., 2019), however, did not yield statistically significant improvements in periodontal parameters in the test group. On the other hand, a recent study have shown that the repeated application of diode laser on titanium implants has eradicated all the microorganisms in more than two-third of the samples without changing the quality of the implant surface (Wawrzyk et

al., 2021a). In the same context, Mettraux and co-workers (2016) showed that the repeated diode laser application following mechanical debridement in the treatment of peri-implantitis lesions resulted in a significant improvement in the periodontal parameters for at least two years. Moreover, temperature rise above critical threshold of 10 ℃ after 18 seconds of application (Sennhenn-Kirchner et al., 2007, Tavares et al., 2017) could be an associated issue of concern. For example, the application of diode laser for 60 seconds in one study (Tenore et al., 2020) brings about more heat that could have jeopardized the implant and surrounding peri-implant tissues (Geminiani et al., 2012). Therefore, special considerations of thermal effect should be taken into account to minimize the heat damage from radiation (Kreisler et al., 2003). The optic fiber diameter, which influences the power density and amount of energy released during laser application, could have possibly altered the anti-inflammatory effects of the diode laser (Radvar et al., 1996). Nevertheless, diode laser has been safely used for peri-implant soft tissue modification and uncovering of submerged dental implants without untoward alteration to titanium implant surfaces compared to other types of lasers or settings (Romanos et al., 2000). Moreover, no adverse effects such as swelling, pain or discomfort were detected following the adjunctive use of diode laser with mechanical debridement in the treatment of the peri-implant diseases (Mettraux et al., 2016). The antimicrobial effect of diode laser has also been evaluated in different implant surfaces and materials. The findings suggest that the diode laser can decontaminate several types of implant surfaces such as hydroxyapatite-coated, plasma-sprayed, acid-etched, and sandblasted titanium surfaces. The required power density to generate a sufficient bactericidal effect is determined by surface characteristics (Kreisler et al., 2003). When evaluating the effect of diode laser on different materials utilized for dental implant constructions such as zirconia and porcelain, the laser operation effectively eliminated bacteria from the surfaces, regardless of the exposure period. Moreover, diode laser irradiation on healing abutments has markedly eliminated the predominant pathogenic bacteria and

accelerated wound healing without any no harmful effects on the evaluated implant material (Wawrzyk et al., 2021b, Wawrzyk et al., 2021c).

It remains unclear whether removal or retention of the prosthetic supra-structure, implant surface characteristics or implant design have influenced the treatment outcomes reported in this review. This is as only one study (Sanchez-Martos et al., 2020a) has clearly reported the removal of the prosthesis to allow adequate access for peri-implant debridement and only one study (Sanchez-Martos et al., 2020a) has provided information on implant system. The limited number of included studies, therefore, did not allow an adequate assessment of the potential benefits of prosthesis removal or determine whether the presence of machined or moderately roughened implant surface have any influence on the treatment outcomes.

All the included studies have shown a reduction in the bleeding in probing; however, the data reported some heterogenicity between them. After a short follow-up period of 3 months, it appeared that using lasers in conjunction with non-surgical therapy could reduce the bleeding on probing. This could be explained by the tissue or vaporization that occurs following laser treatment, and it could also reflect the fact that long-term tissue inflammation control may be linked to the maintenance program rather than the active and/or adjunctive treatment itself.

6.4 Agreements and disagreements with other systematic reviews

The outcomes of using lasers of different wavelengths in the management of peri-implant diseases have been reported in several narrative and systematic reviews (Mattar et al., 2021, Lin et al., 2018, Shahmohammadi et al., 2021, Saneja et al., 2020, Choe et al., 2021, Pisano et al., 2021, Ashnagar et al., 2014), but the outcomes of using diode laser in the management of peri-implant mucositis was reported in two systematic reviews (Albaker et al., 2018, Sanchez-Martos et al., 2020b). Both reviews (Albaker et al., 2018, Sanchez-Martos et al., 2020b) included studies that evaluated the adjunctive use of both photodynamic therapy and diode

laser of different wavelengths and showed that both adjunctive therapies did not provide additional benefits, in agreement with our findings. However, the present review followed a rigorous search strategy and included only RCTs that met stringent criteria having a test group in which implant sites with peri-implant mucositis were treated with mechanical debridement and diode laser (810 nm and 980 nm) and a control group in which sites were treated with mechanical debridement alone. A quantitative analysis of outcomes related to changes in periodontal parameters was also reported. Nevertheless, a number of limitations primarily related to the small number of studies and the heterogeneity across the studies included in the present review should be noted. In particular, heterogeneity in terms of implant locations, surface characteristics, typed of curettes and laser settings need to be acknowledged. Moreover, microbiologic, cost-effectiveness and patient reported outcomes were not analyzed in this review due to lack of or limited information.

7. CONCLUSIONS

In the management of peri-implant mucositis, the combined use of diode laser and mechanical debridement have positive short-term effect on periodontal parameters but any additional clinical advantage over mechanical debridement alone is still not clear. Long-term, well-designed RCTs are still needed to substantiate the clinical benefits of using diode laser as an adjunctive therapy in the management of peri-implant mucositis.

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9. APPENDICES

APPENDEX 1

PRISMA 2020 for abstract checklist

Table 1

Section and topic	Item #	Checklist item	Location where item is reported
Title			
Title	1	Identify the report as a systematic review.	
Abstract			
Abstract	2	See the PRISMA 2020 for Abstracts checklist (table 2).	
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesise results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesised results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	
Results			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram (see fig 1).	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesised results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	
Other information			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code, and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

PRISMA 2020 for abstract checklist

Table 2

Section and topic	Item #	Checklist item
Title		
Title	1	Identify the report as a systematic review.
Background		
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.
Methods		
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.
Synthesis of results	6	Specify the methods used to present and synthesise results.
Results		
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).
Discussion		
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).
Interpretation	10	Provide a general interpretation of the results and important implications.
Other		
Funding	11	Specify the primary source of funding for the review.
Registration	12	Provide the register name and registration number.

*This abstract checklist retains the same items as those included in the PRISMA for Abstracts statement published in 2013,[54] but has been revised to make the wording consistent with the PRISMA 2020 statement and includes a new item recommending authors specify the methods used to present and synthesise results (item #6).