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Photobiomodulation in dental extraction therapy:

Postsurgical pain reduction and wound healing

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Abstract

Background.—This scoping review and analysis were designed to assess the amount of time spent delivering photobiomodulation (PBM) light therapy after dental extraction to improve postoperative pain and wound healing.

Types of Studies Reviewed.—The scoping review was performed according to the Cochrane Collaboration and Preferred Reporting Items for Systematic Reviews and Meta-Analyses criteria. Publications were specific for human randomized controlled clinical trials, PBM after dental extraction therapy, and related clinical outcomes. Online databases searched included PubMed, Embase, Scopus, and Web of Science. Analyses were conducted to analyze the prescribed intervals of time (seconds) per application of PBM.

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Results.—Of the 632 studies initially identified, 22 studies fulfilled the inclusion criteria. Postoperative pain and PBM were reported in 20 articles for 24 treatment groups, with treatment times ranging from 17 through 900 seconds and wavelengths from 550 through 1,064 nm. Clinical wound healing outcomes were reported in 6 articles for 7 groups with treatment times ranging from 30 through 120 seconds and wavelengths from 660 through 808 nm. PBM therapy was not associated with adverse events.

Conclusions and Practical Implications.—There is future potential to integrate PBM after dental extraction therapy to improve postoperative pain and clinical wound healing. The amount of time spent delivering PBM will vary by wavelength and the type of device. Further investigation is needed to translate PBM therapy into human clinical care.

Keywords

Laser; laser therapy; low-level light therapy; tooth extraction; pain management, facial pain; oral surgery procedures; dentistry; photobiomodulation

Photobiomodulation (PBM) therapy is a nonthermal, nonionizing treatment of red and near-infrared light.^{1,2} PBM applications typically involve laser wavelengths from 600 through 1,000 nm. Incorporating PBM as an adjunctive therapy can promote wound healing, reduce inflammation, and provide analgesia. Dentistry research groups have documented PBM applications to improve dental postextraction pain and wound healing.^{3–6} The amount of time spent delivering PBM should be adjusted, as protocols vary by wavelength and between devices.⁷ PBM can be applied safely by optimizing laser settings (irradiation parameters) that are calibrated for the optical properties of alveolar bone and soft tissues.⁸

PBM's photochemical effects transmit light through various tissue types and tissue optical properties.^{8–11} The PBM mechanisms are categorized as intracellular, cell membrane receptors, or extracellular components. Intracellular mechanisms involve the absorption of PBM wavelengths via cytochrome c oxidase, which is contained in the respiratory chain located within the mitochondria.¹² It is hypothesized that PBM light energy is absorbed by cytochrome c oxidase,¹³ leading to enhancement of enzyme activity,¹⁴ electron transport,¹⁵ increasing mitochondrial respiration, and adenosine triphosphate production.¹² By altering the cellular redox state, PBM can activate numerous intracellular signaling pathways, including transcription factors concerned with cell proliferation, survival, tissue repair, and healing.^{12,15} The cell membrane receptor mechanism involves PBM modulation of photosensitive ion transporters and cell receptors on the cell membrane, such as Opsins 2–4, *TRPV1*, *AHR*, and *P2X7*.^{16,17}

The extracellular mechanisms can lead to expected therapeutic results^{1,2,18} that directly photoactivate latent transforming growth factor $\beta 1$ (TGF- $\beta 1$) via a redox-mediated physiochemical process.^{19–24} TGF- $\beta 1$ is a pluripotent family of cytokines,^{22,25} significantly involved as multifunctional growth factors for reepithelialization, inflammation, angiogenesis, and granulation tissue formation during wound healing.^{20,22,25} Specific PBM wavelengths predictably upregulate signaling of TGF- $\beta 1$,^{19–21,23,24} thus affecting keratinocyte function and migration, which is essential to wound reepithelialization.²⁵ There

is evidence to support that TGF- β 1 will appear immediately after PBM treatment, which indicates activity from degranulating platelets in the serum of freshly wounded tissues.^{19,23}

PBM applications in dentistry are guided by randomized controlled trials, systematic reviews, and recommendations from international associations.^{26–30} These bodies of evidence can help the clinician determine the amount of PBM necessary to safely achieve a desired effect. The purpose of our scoping review was to examine emerging evidence for PBM, tooth extraction, pain discomfort, and wound healing. Scoping reviews can identify, assess, and map the available evidence, inform of different types of practice in a specific field, and report on ways that research has been conducted.^{31–34} The aim of our scoping review was to summarize time (seconds) and irradiation settings prescribed for PBM after dental extraction therapy to improve postoperative pain and wound healing. These findings will inform clinicians about available evidence and drive future research without guiding clinical decision making.

METHODS

We conducted a scoping review and irradiation parameter analyses according to the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines.³⁵ The Population, Intervention, Comparison, Outcomes question formulated was as follows: In patients receiving dental extraction therapy (P), does the amount of time prescribed for PBM therapy (I), compared with placebo PBM therapy(C), differ by wavelength for postoperative pain and wound healing (O)? We conducted a detailed review of the literature from January 1, 1970, through June 1, 2022, in the following databases: National Library of Medicine PubMed (MEDLINE), Elsevier Embase, Scopus, and Web of Science. The comprehensive search strategy is available via PROSPERO (registration CRD42022341395). We used the Cochrane Risk of Bias tool for randomized controlled trials (Cochrane RoB 2.0) to assess bias.

The inclusion criteria were

- human prospective randomized controlled trials comparing PBM therapy and a placebo as an adjunct treatment after dental extraction surgery
- studies that reported PBM protocols for clinical outcomes of pain and clinical wound healing
- test groups using a single PBM system at the same laser wavelength throughout the entire treatment
- studies reporting the following irradiation parameters: wavelength (nm), treatment time (seconds), amount of contact points per visit, and the total amount of visits
- studies reporting adverse events, safety, and efficacy
- statistical analysis

The exclusion criteria were

- nonhuman studies
- cohort, case-control, case series, expert opinion, and review studies
- inadequate site standardization
- use of multiple laser systems at different wavelengths or the same PBM system at varying wavelengths
- no placebo or control group
- non-English language

Analysis and data synthesis

We created an electronic data conversion form (Microsoft Excel) to include author, year, wavelength (nm), laser power (W), beam area spot size (cm²), treatment time per point (seconds), irradiance or power (W/cm²), energy dose (J), and fluence (J/cm²). Notations were made if data were misreported or corrected and if values were not reported and were added via synthesis (Table 1). We calculated fluence (J/cm²) as (power × time)/area spot size, energy (J) as power × time, power density (W/cm²) as power/area spot size, and spot size (cm²) as $\pi(\text{radius } 1 \times \text{radius } 2)$, noting that many laser diode beams are elliptical and not round. As applicable, we generated and plotted the mean, median, mode, and upper and lower quartile ranges. We applied wavelength (nm)-specific analyses of irradiation parameters, when possible, to avoid bias caused by the difference in effect.

RESULTS

The literature search is detailed in Figure 1. The search strategy resulted in a total of 632 articles. We identified 67 articles after reviewing titles and abstracts for full-text assessment. We excluded 45 articles for not fulfilling the inclusion and exclusion criteria (Figure 1). We included 22 articles^{1,3–6,36–52} for the review and analysis (Tables 1 and 2). Postoperative pain and PBM were reported in 20 articles with 24 treatment groups (Table 1). Red visible wavelength devices (550–660 nm) were used with 4 articles and 5 treatment groups. PBM treatment times ranged from 30 through 60 seconds per application point, depending on the protocol (Figure 2A). Near-infrared devices (780–1,064 nm) were reported in 18 articles and 19 treatment groups, with treatment times ranging from 17 through 900 seconds per application point (Figure 2B). Some articles had multiple treatment arms testing both red visible and near-infrared wavelengths.

Clinical wound healing outcomes were reported in 6 articles and 7 treatment groups (Table 2). Of the 6 wound healing articles, 4 reported for PBM and soft-tissue wound healing,^{4,36,46,48} and 2 reported for PBM and bone-tissue wound healing^{3,52} (Table 2). Soft-tissue wound healing was reported for both red visible and near-infrared devices. Red visible wavelength devices (660 nm) were used with 2 articles and 2 treatment groups, with PBM delivery times ranging from 30 through 60 seconds (Figure 3A). Near-infrared wavelength devices (808–830 nm) were reported in 3 articles and 3 treatment groups with PBM delivery times ranging from 70 through 120 seconds per application point (Figure 3B). Bone-tissue wound healing was reported for near-infrared devices (808 nm) in 2 articles

and 2 treatment groups, with PBM delivery times ranging from 25 through 30 seconds per application (Figure 3C).

Risk of bias assessment

We summarized the risk of bias in each study according to the Revised Cochrane Risk of Bias 2.0 classification from 2019 (Table 3).⁵³ We considered 16 studies as having a low risk of bias, 4 as having a moderate risk of bias, and 2 as having a high risk of bias (Table 3).

Time: irradiation parameter analysis

A total of 22 studies reported laser irradiation parameter settings with respect to time for each indication of PBM. Some groups reported on more than 1 indication and had multiple treatment groups. Twenty studies reported results for pain (Table 1), and 6 studies reported results for wound healing (Table 2). Of the 6 studies that reported on wound healing, 4 defined parameters for soft-tissue healing and 2 for bone-tissue healing (Table 2). Not all studies fully reported the entire panel of irradiation parameters: laser type, laser power (W), beam area and spot size (cm²), treatment time per point (seconds), energy dose (J), fluence (J/cm²), contact points (per visit), and several appointment intervals.

The pain reduction analysis (Table 1) for treatment time included 20 studies, with reporting on red visible wavelength devices in 4 articles and 5 treatment groups (Figure 2A) and on near-infrared wavelengths in 18 articles and 19 treatment groups (Figure 2B). The reports on red visible devices included the following irradiation parameters: treatment times, 25 through 60 seconds; wavelength, 550 through 660 nm; laser power, 0.02 through 0.1 W; beam area and spot size, 0.028 through 0.05 cm² (3 groups); energy dose, 2.5 through 6 J (4 groups); fluence, 5 through 106 J/cm² (3 groups); contact points, 1 through 4; and appointment intervals, 1 and 2 (Figure 2A). The reports on near-infrared devices included the following irradiation parameters: treatment time, 17.1 through 900 seconds; wavelengths, 780 through 1,064 nm; laser power, 0.04 through 1 W; beam area and spot size, 0.01 through 3.2 cm² (14 groups); energy dose, 2.1 through 180 J (17 groups); fluence, 2 through 212 J/cm² (15 groups); contact points, 1 through 12; and appointment intervals, 1 through 5 (Figure 2B).

The wound healing analysis (Table 2) included 6 studies, with reports on soft-tissue healing for red visible wavelengths in 2 studies and 2 groups (Figure 3A) and on near-infrared devices in 3 studies and 3 groups (Figure 3B). Bone-tissue healing was reported using near-infrared devices in 2 studies and 2 groups (Figure 3C). Reports on soft-tissue wound healing with red visible devices included the following irradiation parameters: treatment times, 30 through 60 seconds; wavelength, 660 nm; laser power, 0.02 through 0.025 W; beam area and spot size, (none); energy dose, 6 J (1 group); fluence, (none); contact points, 1 through 3; and appointment intervals, 1 through 3 (Figure 3A). Reports on near-infrared devices included the following irradiation parameters for 3 articles and 3 groups: treatment time, 70 through 120 seconds; wavelengths, 808 through 830 nm; laser power, 0.02 through 0.04 W; beam area and spot size, 0.28 cm² (2 groups); energy dose, 2.8 through 6 J; fluence, 2.14 through 100 J/cm² (2 groups); contact points, 1 through 5; and appointment intervals, 1 through 4 (Figure 3B). Reports on bone-tissue healing with near-infrared devices included

the following irradiation parameters in 2 articles and 2 groups: treatment time, 25 through 30 seconds; wavelength, 808 nm; laser power, 0.1 W; beam area and spot size, 0.028 through 0.04 cm²; energy dose, 2.5 through 3 J; fluence, 75 through 89 J/cm²; contact points, 5; and appointment intervals, 5 (Figure 3C).

DISCUSSION

In our scoping review of available evidence, we evaluated the use of PBM in postsurgical dental extraction therapy and determined that time spent delivering PBM can range from 17.1 through 900 seconds per treatment application. The amount of time prescribed for each PBM protocol differed according to the wavelengths reported. Delivering PBM light after extraction can influence pain reduction and clinical wound healing. The specific amount of time spent delivering PBM to improve pain and wound healing differs per device and wavelength (Tables 1 and 2, Figures 2 and 3). Achieving these outcomes is possible and requires further investigation for red and near-infrared wavelengths. Future research is needed to better understand the wide heterogeneity reported in the available evidence of this review, specifically for PBM time delivery and irradiation parameter settings.

The standard for postoperative dental extraction therapy requires solutions that promote healing, prevent complications, and provide comfort. Dentistry is transitioning away from dispensing narcotics due to increased rates of opioid misuse.^{54–56} Practitioners have adopted alternatives by prescribing analgesics, corticosteroids, and antibiotics. Although these medications are effective nonnarcotic treatment options, they may not be viable for all patient populations. This can be due to patient preference, noncompliance, or history of medical compromise. The results of our scoping review provide a summary of emerging evidence that can be investigated further to support the use of PBM in dental extraction therapy. There is potential to improve the standard of postoperative care for dental extractions by expanding future PBM research through recognized dose-escalation trial formats.^{57–59}

We selected dental extraction therapy for our analysis because it is a procedure that is well documented in the literature.^{60–63} It is well understood that complications from dental extractions can present as excessive inflammation, postoperative surgical pain, swelling, and trismus.⁶⁴ A dental extraction procedure will initiate biological events that immediately alter soft- and hard-tissue structures.⁶⁵ Extraction therapies will release inflammatory mediators, provoke tissue damage, and activate nociceptors, which can be altered by PBM.^{3,6,42,43,49,50,52,66}

Translating the findings reported in this review may pose challenges for future investigators. We determined that the amount of time spent delivering PBM ranged from 17.1 through 900 seconds per application for wavelengths ranging from 550 through 1,064 nm (Tables 1 and 2, Figures 2 and 3). In the ideal circumstance, the amount of time spent delivering PBM will predictably stimulate a biological effect at the targeted site. To further explore the potential for achieving a PBM biological effect on tissue, future research should investigate the cumulative amount of time spent delivering PBM with specific irradiation parameters

(Figures 2 and 3). This will allow a greater understanding of the behavioral characteristics specific to each wavelength and each device.

Additional investigations are necessary to determine the appointment intervals required for PBM light delivery after a dental extraction procedure. The results of our review reported PBM protocols requiring from 1 through 5 postoperative appointments (Tables 1 and 2, Figures 2 and 3). Establishing a PBM protocol with multiple PBM treatment visits may not be feasible in the nonresearch setting because of scheduling limitations and patient availability. Despite this wide range of PBM appointment intervals (Figures 2 and 3), several studies reported promising pain reduction results with a single PBM application on the day of surgery.^{4,6,47,50} The amount of time spent delivering PBM for these studies with a single intervention varied by device from 30 through 73 seconds per application. The total cumulative treatment time for a single appointment in this group ranged from 60 through 438 seconds. In addition, 1 study that applied PBM immediately after extraction showed improvements in soft-tissue wound healing and a total treatment time of 60 seconds in 1 application.⁴

The results from our analysis reported on protocols describing the placement of the PBM probe at different anatomic locations. Clinical sites varied from external points of contact, internal points of contact, being in direct contact, or having a fixed distance from the anatomy (Tables 1 and 2, Figures 2 and 3). An optimal amount of PBM light can be delivered at the intended target site and requires the dose distribution at the target tissue to ensure adequate coverage of the intended pathology. Tissue optical properties can vary spatially due to the presence of optical nonuniformities. These properties can vary due to hemodynamic and metabolic processes that occur between tissue types with different biological structures and as a function of wavelength.^{67,68} It is possible to model total tissue dose distribution over the entire tissue volume by using the diffusion approximation equation for light in tissue.^{69,70} PBM devices are manufactured with distinct specifications for the shape of the lens and the beam area and spot size of the handheld probe. It is important to recognize these details as they will help clinicians better deliver PBM light, fluence, and energy.

Prescribing a PBM delivery protocol can follow a predictable and safe evidence-based approach. An animal study has helped determine therapeutic dose limits, biological safety, and molecular pathways involved with phototoxicity.⁷¹ Human tissue optical properties vary from person to person and are characterized by coefficients of absorption, scattering, and depth of penetration and attenuation.^{9,72} PBM can be prescribed via the following parameters: wavelength (nm), laser power (W), treatment time (seconds), beam area and spot size (cm²), and fluence (J/cm²).² Optimizing these settings to specific tissue optical properties will deliver a light dose received at the intended target site (fluence, J/cm²).^{18,66,73,74} Accurately quantifying irradiation parameters will guide the prescription formula for an effective PBM treatment.

Ng and colleagues'⁸ 2018 article focused on the amount of energy loss when laser energy penetrates through human alveolar bone. They investigated a total of 27 extraction sockets and determined that each millimeter of bone thickness amounted to a 6.81% reduction in

laser energy. Understanding how to prescribe for depth of penetration (attenuation) can guide dosing protocols toward biomolecular targets like the hemoglobin coefficient of absorption.¹¹ Specifically, when oxygen is coupled to hemoglobin, the 500 through 600 nm red visible wavelength laser penetration peaks at a shallow depth of 0.6 mm, maintaining a steady decline through 2.0 mm. Asimov and colleagues¹¹ also noted that when oxygen is decoupled from hemoglobin, the laser at the 800 nm near-infrared range penetrates at 2.0 mm depth and remains steady through 3.0 mm.

Our scoping review has limitations in the variation in the amount of time spent delivering PBM and the wide range of wavelengths (Tables 1 and 2, Figures 2 and 3). Given the unique characteristics of each type of device and wavelength, the total number of validated PBM protocols for pain reduction and wound healing that are available in the published databases is limited. Substantial efforts are needed to standardize PBM therapy by reporting all irradiation parameters (Tables 1 and 2, Figures 2 and 3). This will allow future research groups to validate any outcomes with further investigation.

Another limitation of this review was the inconsistent standardization of dental extraction sites and the array of pain and wound healing indexes used for the PBM trials reported. The pain outcomes reported included 14 studies reporting on mandibular third molars, 1 study on mandibular molars, 4 studies on both maxillary and mandibular third molars, and 1 study on maxillary and mandibular premolars. The 4 soft-tissue wound healing studies included mandibular molars, maxillary and mandibular teeth, and mandibular third molars. Both bone tissue studies reported on mandibular molars.

Pain reduction and wound healing indexes were not standardized in type and appointment intervals. Although 15 pain studies used a visual analog pain scale, measurement intervals were not consistent among all the groups. The remaining 5 pain studies used a visual numerical scale, Giles scale, Likert scale, pain analog scale, and the Universal Pain Assessment Tool scale. The soft-tissue healing indexes were not standardized, with each study using a different type of measurement with varying assessment intervals. The bone-tissue wound healing analyses were consistent with micro-computed tomography and histology analysis at the time of biopsy on days 40 and 45.

A challenge realized from this analysis was that several PBM settings should have been reported by the authors. We recognize that multiple PBM settings (power, beam area and spot size, energy, fluence) were unique to our analysis, as they are necessary to calculate the amount of light delivered. However, we also acknowledge that these criteria may be considered trade secrets, as the manufacturer does not always release device specifications. Knowledge of these settings is necessary for scientific validation in a clinical setting. A complete understanding of these criteria will guide clinical calculations for PBM light delivery that are needed to accurately reproduce a protocol. Authors were not contacted for these specifications to highlight the lack of reporting PBM settings (Tables 1 and 2). A complete analysis of all settings was only possible with bone-tissue wound healing (Figure 3C).

CONCLUSION

To our knowledge, this is the first PBM scoping review to present a summary analysis of available evidence for time (seconds) and irradiation parameters prescribed for PBM after dental extraction therapy to improve postoperative pain and wound healing. The results of this study determined that the amount of time prescribed for PBM differs by wavelength for postoperative pain and wound healing after tooth extraction. Further studies are needed before PBM can be introduced to clinical practice after a routine dental extraction procedure.

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ABBREVIATION KEY

AlGaAs Aluminum gallium arsenide

AsGaAl	Arsenide gallium aluminium
C	Contact
E	Extraoral
GaAlAs	Gallium aluminum arsenide
GaAs	Gallium arsenide
I	Intraoral
NC	Noncontact
Nd:YAG	Neodymium-doped yttrium aluminum garnet
PBM	Photobiomodulation
TGF- β1	Transforming growth factor β 1
VAS	Visual analog scale

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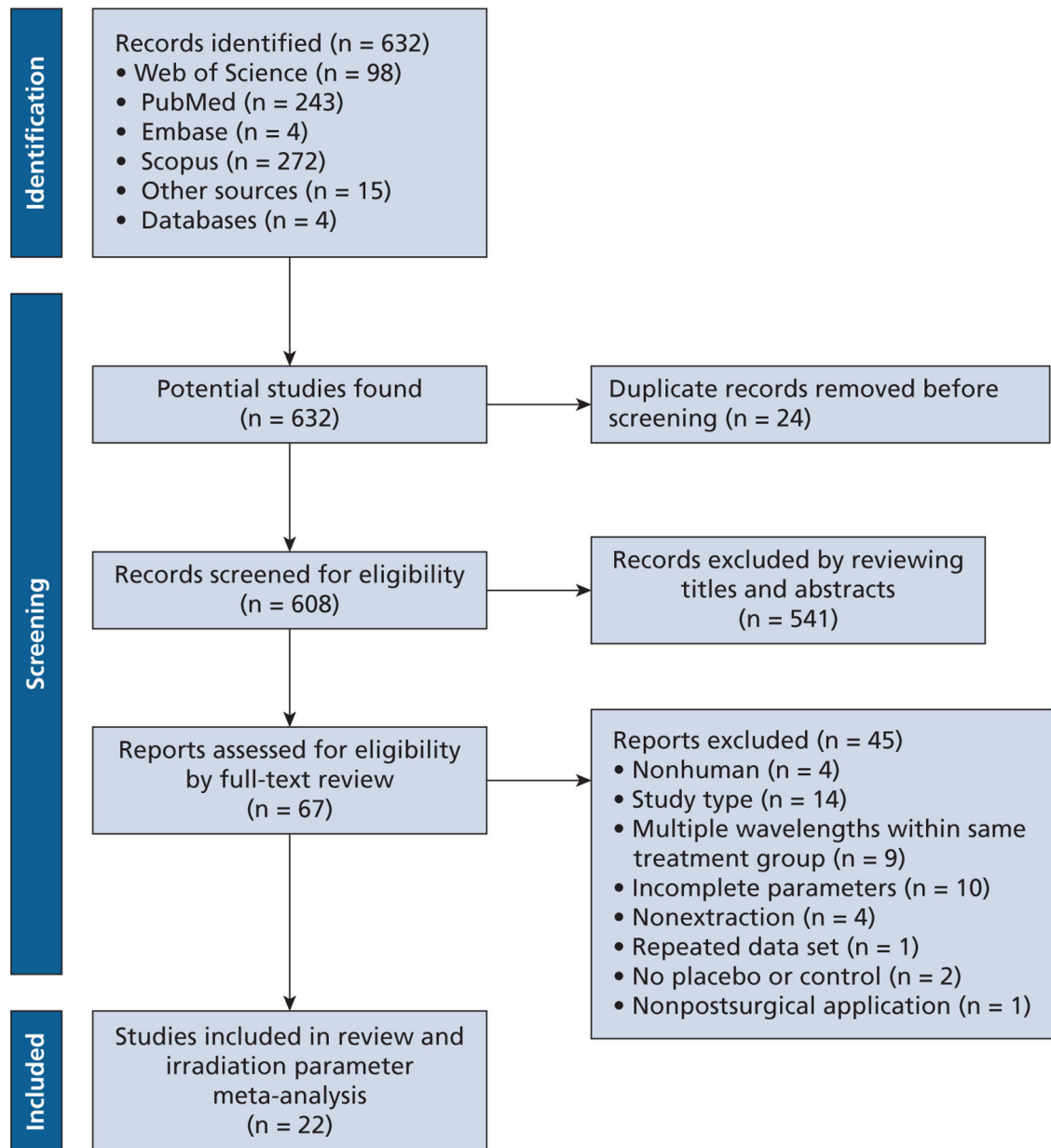
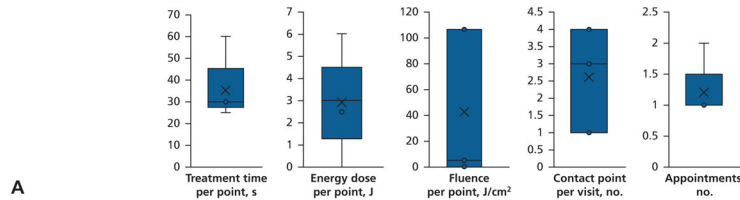


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flowchart of study search and selection process.³⁵

Author	Year	Wavelength, mm	Laser type	Laser power, W	Beam area and spot size, cm ²	Treatment time, per point, s	Energy dose per point, J	Fluence, J/cm ²	Clinical site	Contact points per visit, no.	Appointment, no.	Appointment days
Sierra and Colleagues ⁵⁶	2016	660	–*	0.1 [†]	0.028 [‡]	30	3	106	I, C	4	1	1
Sierra and Colleagues ⁵⁶	2016	660	–	0.1 [†]	0.028 [‡]	30	3	106	E, C	4	1	1
Farhadi and Colleagues ⁶⁷	2017	550	–	0.1 [†]	0.5	25	2.5	5	I, C	1	1	1
Ahrari and Colleagues ³⁶	2020	660	GaAlAs	0.02 [†]	–	30	6	–	E, NC	3	2	1, 3
Salem ⁴	2020	660	–	0.025 [‡]	–	60	–	–	I, NC	1	1	1



Author	Year	Wavelength, mm	Laser type	Laser power, W	Beam area and spot size, cm ²	Treatment time, per point, s	Energy dose per point, J	Fluence, J/cm ²	Clinical site	Contact points per visit, no.	Appointment, no.	Appointment days
Fernando and Colleagues ³⁸	1993	830	–*	0.03	–	120	4	–	I, C	1	1	1
Mozzati and Colleagues ⁸⁸	2011	904	GaAs	0.2 [†]	1	900 [†]	180	180	I, C	1	1	4
Lopez and Colleagues ¹	2012	810	AsGaAl	0.4	3.2 [‡]	32	12.8	4	I, C	1	1	1
Mozzati and Colleagues ⁶⁹	2012	904	GaAs	0.2 [†]	1	900 [†]	180	180	I, C	1	1	3
Paschoal and Santos-Pinto ⁷⁰	2012	830	GaAlAs	0.1	0.01 [†]	17	1.7	170 [†]	I, NC	3	3	1, 2, 3
Ferrante and Colleagues ⁷¹	2013	980	–	0.3	–	60	18	–	I, NC; E, C	3	2	1, 2
Alan and Colleagues ⁷²	2016	810	GaAlAs	0.3	–	40	12	–	E, C	1	2	1, 2
Pedreira and Colleagues ⁵⁷	2016	808	AlGaAs	–	–	30 [‡]	–	2 [†]	E, C, I, C	12	4	1, 3, 5, 7
Sierra and Colleagues ⁵⁶	2016	808	–	0.1 [†]	0.028 [‡]	30	3	106	I, C	4	1	1
Sierra and Colleagues ⁵⁶	2016	808	–	0.1 [†]	0.028 [‡]	30	3	106	E, C	4	1	1
Feslihan and Eroglu ⁷³	2019	810	GaAlAs	0.3	3	60	18 [‡]	6	E, C	1	2	1, 2
Ahrari and Colleagues ³⁶	2020	810	GaAlAs	0.02 [†]	0.28	30	6	2.14 [†]	E, NC	3	2	1, 3
Santos and Colleagues ³⁸	2020	780	–	0.07 [†]	0.04	30	2.1 [‡]	52.5	I, C	5	1	1
Da Silva and Colleagues ³⁷	2021	808	–	0.04	0.28	70	2.8	100	I, C	5	4	0, 7, 14, 21
Isolan and Colleagues ⁵	2021	808	GaAlAs	0.05 [†]	0.4	73 [†]	11	9.125 [†]	I, C	6	1	1
Momeni and Colleagues ⁵	2021	940	–	0.5	1.5 [‡]	30	15	10	I, NC	3	1	2
Scarano and Colleagues ⁵⁴	2021	1064	Nd:YAG	1	–	17.1 [†]	–	–	I, NC	7	5	1, 2, 4, 9, 14
Hadad and Colleagues ⁵⁵	2022	810	GaAlAs	0.1	0.0283 [‡]	60	6	212	I, C	4	1	1
Le and Colleagues ⁷⁴	2022	810	GaAlAs	0.43 [‡]	3.2 [‡]	30	12.8	4	I, NC	1	2	1, 2

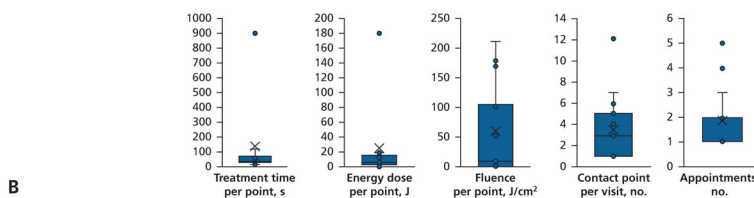
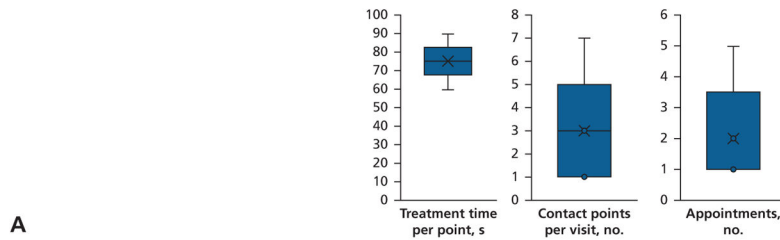


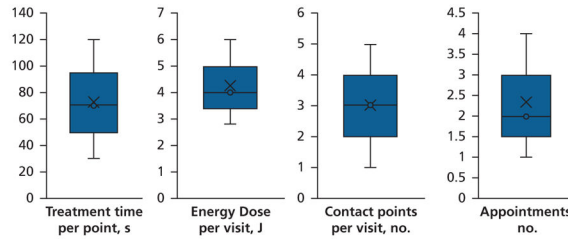
Figure 2. Pain, analyses for time and irradiation parameters: 24 treatment groups reported from 20 studies. **A.** Red visible light wavelengths, 550 through 660 nm. **B.** Near-infrared wavelengths, 780 through 1,064 nm. AlGaAs: Aluminum gallium arsenide. AsGaAl: Arsenide gallium aluminium. C: Contact. E: Extraoral. GaAlAs: Gallium aluminium arsenide. GaAs: Gallium arsenide. I: Intraoral. NC: Noncontact. Nd:YAG: Neodymium-doped yttrium aluminum garnet. * –: A value that cannot be derived from other reported values. † Indicates value that was initially misreported and corrected by the authors’ calculations. ‡ Indicates value was not reported in the literature and was calculated by the authors with values given in the article.

Author	Year	Wavelength, mm	Laser type	Laser power, W	Beam area and spot size, cm ²	Treatment time, per point, s	Energy dose per point, J	Fluence, J/cm ²	Clinical site	Contact points per visit, no.	Appointment, no.	Appointment days
Ahrari and Colleagues ³⁶	2020	660	GaAlAs	0.02 [†]	—*	30	6	—	E, NC	3	2	1, 3
Salem ⁴	2020	660	—	0.025 [†]	—	60	—	—	I, NC	1	1	1



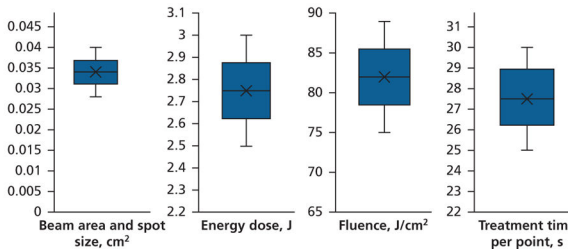
A

Author	Year	Wavelength, mm	Laser type	Laser power, W	Beam area and spot size, cm ²	Treatment time, per point, s	Energy dose per point, J	Fluence, J/cm ²	Clinical site	Contact points per visit, no.	Appointment, no.	Appointment days
Fernando and Colleagues ³⁸	1993	830	—	0.03	—	120	4	—	I, C	1	1	1
Ahrari and Colleagues ³⁶	2020	810	GaAlAs	0.02 [†]	0.28	30	6	2.14 [†]	E, NC	3	2	1, 3
Da Silva and Colleagues ³⁷	2021	808	—	0.04	0.28	70	2.8	100	I, C	5	4	0, 7, 14, 21



B

Author	Year	Wavelength, mm	Laser type	Laser power, W	Beam area and spot size, cm ²	Treatment time, per point, s	Energy dose per point, J	Fluence, J/cm ²	Clinical site	Contact points per visit, no.	Appointment, no.	Appointment days
Romao and Colleagues ³	2015	808	GaAlAs	0.1 [†]	0.04	30	3	75	I, C	5	5	1, 3, 5, 7, 14
Rosero and Colleagues ³⁹	2020	808	GaAlAs	0.1	0.028	25	2.5	89	I, C	5	5	1, 3, 5, 7, 14



C

Figure 3. Wound healing, analyses for time and irradiation parameters. **A.** Red visible light wavelengths, soft tissue, 660 nm. **B.** Near-infrared wavelengths, soft tissue, 808 through 830 nm. **C.** Near-infrared wavelengths, bone tissue, 808 nm. C: Contact. E: Extraoral. GaAlAs: Gallium aluminum arsenide. I: Intraoral. NC: Noncontact. * —: A value that cannot be derived from other reported values. † Indicates value that was initially misreported and corrected by the authors' calculations.

Summary of characteristics in studies reporting on pain

Table 1.

AUTHOR	YEAR	WAVELENGTH, NM	LASER TYPE	LASER POWER, W	BEAM AREA AND SPOT SIZE, cm ²	TREATMENT TIME PER POINT, S	ENERGY DOSE PER POINT, J	FLUENCE, J/cm ²	CLINICAL SITE	CONTACT POINTS, NO.	APPOINTMENT INTERVALS, NO.	APPOINTMENT DAYS	SURGICAL SITE	PAIN SCALE
Fernando and Colleagues ³⁶	1993	830	—*	0.03	—	120	4	—	Intraoral, contact	1	1	1	Mandibular third molar	Giles
Mozzati and Colleagues ³⁷	2011	904	Gallium arsenide	0.2 [†]	1	900 [†]	180	180	Intraoral, contact	1	1	4	Maxillary and mandibular molar	VAS [‡]
Lopez and Colleagues ¹	2012	810	Gallium aluminum arsenide	0.4	3.2 [§]	32	12.8	4	Intraoral, contact	1	1	1	Mandibular third molar	VAS
Mozzati and Colleagues ³⁸	2012	904	Gallium arsenide	0.2 [†]	1	900 [†]	180	18 ^{‡‡}	Intraoral, contact	1	1	3	Maxillary and mandibular molar	VAS
Paschoal and Santos-Pinto ³⁹	2012	830	GaAlAs [¶]	0.1	0.01 [†]	17	1.7	170 [†]	Intraoral, noncontact	3	3	1–3	Maxillary and mandibular premolar	VAS
Ferrante and Colleagues ⁴⁰	2013	980	—	0.3	—	60	18 ^{‡‡}	—	Intraoral, noncontact; extraoral, contact	3	2	1, 2	Mandibular third molar	VAS
Alan and Colleagues ⁴¹	2016	810	GaAlAs	0.3	—	40	12	—	Extraoral, contact	1	2	1, 2	Mandibular third molar	VAS
Pedreira and Colleagues ⁴²	2016	808	Aluminum gallium arsenide	—	—	30 [§]	—	2 [†]	Extraoral, contact; intraoral, contact	12	4	1, 3, 5, 7	Mandibular third molar	Pain analog
Sierra and Colleagues ⁴⁵	2016	660	—	0.1 [†]	0.028 ^{§§}	30	3	106	Intraoral, contact	4	1	1	Mandibular third molar	VAS
Sierra and Colleagues ⁴³	2016	660	—	0.1 [†]	0.028 ^{§§}	30	3	106	Extraoral, contact	4	1	1	Mandibular third molar	VAS

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AUTHOR	YEAR	WAVELENGTH, NM	LASER TYPE	LASER POWER, W	BEAM AREA AND SPOT SIZE, cm ²	TREATMENT TIME PER POINT, S	ENERGY DOSE PER POINT, J	FLUENCE, J/cm ²	CLINICAL SITE	CONTACT POINTS, NO.	APPOINTMENT INTERVALS, NO.	APPOINTMENT DAYS	SURGICAL SITE	PAIN SCALE
Sierra and Colleagues ⁴³	2016	808	-	0.1 [†]	0.028 [§]	30	3	106	Intraoral, contact	4	1	1	Mandibular third molar	VAS
Sierra and Colleagues ⁴³	2016	808	-	0.1 [†]	0.028 [§]	30	3	106	Extraoral, contact	4	1	1	Mandibular third molar	VAS
Farhadi and Colleagues ⁴⁴	2017	550	-	0.1 [†]	0.5	25	2.5	5	Intraoral, contact	1	1	1	Mandibular third molar	VAS
Feslihan and Eroglu ⁴⁵	2019	810	GaAlAs	0.3	3	60	18 [§]	6	Extraoral, contact	1	2	1, 2	Mandibular third molar	VAS
Ahrari and Colleagues ⁴⁶	2020	660	Aluminum gallium indium phosphide	0.02 [‡]	-	30	6	-	Extraoral, noncontact	3	2	1, 3	Mandibular molar	VAS
Ahrari and Colleagues ⁴⁶	2020	810	GaAlAs	0.02 [‡]	0.28	30	6	2.14 [‡]	Extraoral, noncontact	3	2	1, 3	Mandibular molar	VAS
Salem ⁴	2020	660	-	0.025 [‡]	-	60	-	-	Intraoral, noncontact	1	1	1	Mandibular third molar	Universal Pain Assessment Tool
Santos and Colleagues ⁴⁷	2020	780	-	0.07 [‡]	0.04	30	2.1 [§]	52.5	Intraoral, contact	5	1	1	Mandibular third molar	Modified VAS
Da Silva and Colleagues ⁴⁸	2021	808	-	0.04	0.28	70	2.8	100	Intraoral, contact	5	4	0, 7, 14, 21	Maxilla and mandibula	VAS
Isolan and Colleagues ⁶	2021	808	GaAlAs	0.05 [‡]	0.4	73 [‡]	11	9.125 [‡]	Intraoral, contact	6	1	1	Maxillary and mandibular third molar	VAS
Momeni and	2021	940	-	0.5	1.5 [§]	30	15	10	Intraoral, noncontact	3	1	2	Mandibular third molar	VAS

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AUTHOR	YEAR	WAVELENGTH, NM	LASER TYPE	LASER POWER, W	BEAM AREA AND SPOT SIZE, cm ²	TREATMENT TIME PER POINT, S	ENERGY DOSE PER POINT, J	FLUENCE, J/cm ²	CLINICAL SITE	CONTACT POINTS, NO.	APPOINTMENT INTERVALS, NO.	APPOINTMENT DAYS	SURGICAL SITE	PAIN SCALE
Scarano and Colleagues ⁵	2021	1064	Neodymium-doped yttrium aluminum garnet.	1	-	17.1 [†]	-	-	Intraoral, noncontact	7	5	1, 2, 4, 9, 14	Mandibular third molar	VAS
Hadad and Colleagues ⁵⁰	2022	810	GaAlAs	0.1	0.0283 [§]	60	6	212	Intraoral, contact	4	1	1	Mandibular third molar	VAS
Le and Colleagues ⁵¹	2022	810	GaAlAs	0.43 [§]	3.2 [§]	30	12.8	4	Intraoral, noncontact	1	2	1, 2	Mandibular third molar	Likert

[†] - A value that cannot be derived from other reported values.

[‡] - Indicates value that was initially misreported and corrected by the authors' calculations.

[§] - VAS: Visual analog scale.

[¶] - Indicates value was not reported in the literature and was calculated by the authors with values given in the article.

^{||} - GaAlAs: Gallium aluminum arsenide.

Table 2.

of characteristics in studies reporting on wound healing

YEAR	WAVELENGTH, NM	LASER TYPE	LASER POWER, W	BEAM AREA AND SPOT SIZE, cm ²	TREATMENT TIME PER POINT, S	ENERGY DOSE PER POINT, J	FLUENCE, J/cm ²	CLINICAL SITE	CONTACT POINTS, NO.	APPOINTMENT INTERVALS, NO.	APPOINTMENT DAYS	WOUND HEALING	SURGICAL SITE	DAYS, WOUND HEALING SCALE
1993	830	-*	0.03	-	120	4	-	Intraoral, contact	1	1	1	Soft tissue	Mandibular third molar	0, 7; healing scale
2015	808	GaAlAs [†]	0.1 [‡]	0.04	30	3	75	Intraoral, contact	5	5	1, 3, 5, 7, 14	Bone tissue	Mandibular molar	40; micro-computed tomography, histology
2020	810	Aluminum gallium indium phosphide	0.02 [‡]	0.28	30	6	2.14 [‡]	Extraoral, noncontact	3	2	1, 3	Soft tissue	Mandibular molar	3, 7; degree of healing
2020	660	GaAlAs	0.02 [‡]	-	30	6	-	Extraoral, noncontact	3	2	1, 3	Soft tissue	Mandibular molar	Photos on 3, 7; degree of healing
2020	808	GaAlAs	0.1	0.028	25	2.5	89	Intraoral, contact	5	5	1, 3, 5, 7, 14	Bone tissue	Mandibular molar	45; micro-computed tomography, histology
2020	660	-	0.025 [‡]	-	60	-	-	Intraoral, noncontact	1	1	1	Soft tissue	Mandibular third molar	1, 2, 7; Laundry and Turnbull
2021	808	-	0.04	0.28	70	2.8	100	Intraoral, contact	5	4	0, 7, 14, 21	Soft tissue	Maxilla and mandible	7, 14, 18, 21; alveolar mucosa healing

that cannot be derived from other reported values.

† Gallium aluminum arsenide.

‡ Value that was initially misreported and corrected by the authors' calculations.

Table 3.

Risk of bias assessment of the included studies.

AUTHOR	YEAR	RANDOMIZATION PROCESS	DEVIATIONS FROM THE INTENDED INTERVENTION	MISSING OUTCOME DATA	MEASUREMENT OF THE OUTCOME	SELECTION OF THE REPORTED RESULTS	OVERALL RISE OF BIAS
Fernando and Colleagues ³⁶	1993	Low	Low	Low	Low	Low	Low
Mozzati and Colleagues ³⁷	2011	Low	Low	Low	Low	Low	Low
Lopez and Colleagues ¹	2012	Low	Low	Low	Low	Low	Low
Mozzati and Colleagues ³⁸	2012	Low	Low	Low	Low	Low	Low
Paschoal and Santos-Pinto ³⁹	2012	Low	Low	Some concern	Low	Low	Some concern
Ferrante and Colleagues ⁴⁰	2013	Low	Low	Low	Low	Low	Low
Romao and Colleagues ³	2015	Low	Low	Low	Low	Low	Low
Alan and Colleagues ⁴¹	2016	Low	Low	Low	Low	High	High
Pedreira and Colleagues ⁴²	2016	Low	Low	Low	Low	Low	Low
Sierra and Colleagues ⁴³	2016	Low	Low	Low	Low	Low	Low
Farhadi and Colleagues ⁴⁴	2017	Low	Low	Low	Low	Low	Low
Feshlan and Eroglu ⁴⁵	2019	Low	Low	Low	Low	Low	Low
Ahrari and Colleagues ⁴⁶	2020	Some concern	Low	Low	Low	High	High
Rosero and Colleagues ⁵²	2020	Low	Low	Low	Low	Low	Low
Salem ⁴	2020	Low	Low	Low	Low	Low	Low
Santos and Colleagues ⁴⁷	2020	Low	Low	Low	Low	Low	Low
Da Silva and Colleagues ⁴⁸	2021	Low	Low	Low	Low	Low	Low
Isolan and Colleagues ⁶	2021	Some concern	Low	Low	Low	Low	Some concern
Momeni and Colleagues ⁵	2021	Low	Low	Low	Low	Low	Low
Scarano and Colleagues ⁴⁹	2021	Low	Low	Low	Low	Low	Low
Hadad and Colleagues ⁵⁰	2022	Some concern	Low	Some concern	Low	Low	Some concern
Le and Colleagues ⁵¹	2022	Low	Low	Some concern	Low	Low	Some concern