

Medical Policy



Title: Low-Level Laser Therapy

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Populations	Interventions	Comparators	Outcomes
Individuals: • With increased risk of oral mucositis due to some cancer treatments and/or hematopoietic cell transplantation	Interventions of interest are: • Low-level laser therapy	Comparators of interest are: • Conservative therapy (e.g., oral hygiene, hydration) • Medication	Relevant outcomes include: • Symptoms • Morbid events • Quality of life • Treatment-related morbidity
Individuals: • With carpal tunnel syndrome	Interventions of interest are: • Low-level laser therapy	Comparators of interest are: • Conservative therapy (e.g., physical therapy) • Medication • Surgery	Relevant outcomes include: • Symptoms • Morbid events • Quality of life • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> • With neck pain 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative therapy (e.g., physical therapy) • Medication • Surgery 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With subacromial impingement syndrome 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative therapy (e.g., physical therapy) • Medication • Surgery 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With adhesive capsulitis 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative therapy (e.g., physical therapy) • Medication • Surgery 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With temporomandibular joint pain 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative therapy (e.g., physical therapy) • Medication • Surgery 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With low back pain 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative therapy (e.g., physical therapy) • Medication • Surgery 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With osteoarthritic knee pain 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative therapy (e.g., physical therapy) • Medication • Surgery 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With heel pain (i.e., Achilles tendinopathy, plantar fasciitis) 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative therapy (e.g., physical therapy) • Medication • Surgery 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> • With rheumatoid arthritis 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative care (e.g., exercise) • Medication 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With Bell palsy 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative care (e.g., exercise) • Medication 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity •
Individuals: <ul style="list-style-type: none"> • With fibromyalgia 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative care (e.g., exercise) • Medication 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With chronic nonhealing wounds 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Standard wound care 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Change in disease status • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With lymphedema 	Interventions of interest are: <ul style="list-style-type: none"> • Low-level laser therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Conservative care (e.g., exercise) • Pneumatic compression • Complete decongestive therapy 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity

DESCRIPTION

Low-level laser therapy (LLLT), also called photobiomodulation, is being evaluated to treat various conditions, including, among others, oral mucositis, myofascial pain, joint pain, lymphedema, and chronic wounds.

OBJECTIVE

The objective of this evidence review is to evaluate net health outcomes of low-level laser therapy for treating individuals at increased risk of mucositis and other conditions (e.g., soft tissue injuries, myofascial pain, tendinopathies, nerve injuries, joint pain, lymphedema).

BACKGROUND

Oral Mucositis

Oral mucositis describes inflammation of the oral mucosa and typically manifests as erythema or ulcerations that appear 7 to 10 days after initiation of high-dose cancer therapy. Oral mucositis can cause significant pain and increased risk of systemic infection, dependency on total parenteral nutrition, and use of opioid analgesics.

Treatment

Treatment planning may also need to be modified due to dose-limiting toxicity. There are a number of interventions for oral mucositis that may partially control symptoms but none is considered a criterion standard treatment. When uncomplicated by infection, oral mucositis is self-limited and usually heals within 2 to 4 weeks after cessation of cytotoxic chemotherapy. Low-level laser therapy (LLLT) has been used in cancer therapy-induced oral mucositis in individuals treated with radiotherapy and/or chemotherapy and hematopoietic cell transplantation.

Musculoskeletal and Neurologic Disorders

Musculoskeletal disorder describes a variety of conditions leading to chronic pain and decreased quality of life. Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy and the most commonly performed surgery of the hand. The syndrome is related to the bony anatomy of the wrist. The carpal tunnel is bound dorsally and laterally by the carpal bones and ventrally by the transverse carpal ligament. Through this contained space run the 9 flexor tendons and the median nerve. Therefore, any space-occupying lesion can compress the median nerve and produce the typical symptoms of CTS pain, numbness, and tingling in the distribution of the median nerve. Symptoms of more severe cases include hypesthesia, clumsiness, loss of dexterity, and weakness of pinch. In the most severe cases, individuals experience marked sensory loss and significant functional impairment with thenar atrophy.

Treatment

Several modalities of treatment are used in the management of musculoskeletal pain including medications, immobilization, and physical therapy. The use of LLLT has been investigated for use in musculoskeletal pain conditions. In the case of CTS, mild-to-moderate cases are usually first treated conservatively with splinting and cessation of aggravating activities. Other conservative therapies include oral steroids, diuretics, nonsteroidal anti-inflammatory drugs, and steroid injections into the carpal tunnel itself. Individuals who do not respond to conservative therapy or who present with severe CTS with thenar atrophy may be considered candidates for surgical release of the carpal ligament, using either an open or endoscopic approach. Low-level laser therapy is also used to treat CTS.

Wound Care and Lymphedema

Chronic wounds are wounds that do not improve after 4 weeks or heal within 8 weeks. These include diabetic foot ulcers, venous-related ulcerations, non-healing surgical wounds, and pressure ulcers. They are often found on the feet, ankles, heels, and calves, and on the hips, thighs, and buttocks of those who cannot walk.

Lymphedema is described as swelling in at least 1 leg and/or arm. It is commonly caused by the removal of a lymph node. The resulting blockage of the lymphatic system prevents lymph fluid from draining well, leading to fluid build-up and swelling. Other symptoms can include heaviness

or tightness in the affected limb, restricted range of motion, aching or discomfort, recurring infections, and dermal fibrosis. Risk factors for developing lymphedema after cancer from cancer treatment or from other secondary causes can include older age, obesity, and rheumatoid or psoriatic arthritis.

Treatment

Chronic wound management involves ensuring adequate blood flow to the area, preventing the wound from drying, controlling infections, debriding scarred and necrotic tissue, and managing pain. The standard of care for diabetic foot ulcers includes debridement, dressings, offloading of pressure, infection management, and glycemic control. Lymphedema is typically managed with pneumatic compression, exercise, or complete decompression therapy. Use of LLLT has been investigated for the management of both chronic wounds and lymphedema.

Low-Level Laser Therapy

Low-level laser therapy is the use of red-beam or near-infrared lasers with a wavelength between 600 and 1000 nm and power between 5 and 500 MW. By comparison, lasers used in surgery typically use 300 W. When applied to the skin, LLLT produces no sensation and does not burn the skin. Because of the low absorption by human skin, it is hypothesized that the laser light can penetrate deeply into the tissues where it has a photobiostimulative effect. The exact mechanism of its effect on tissue healing is unknown; hypotheses have included improved cellular repair and stimulation of the immune, lymphatic, and vascular systems.

Low-level laser therapy is being evaluated to treat a wide variety of conditions, including soft tissue injuries, myofascial pain, tendinopathies, nerve injuries, joint pain, and lymphedema.

REGULATORY STATUS

Table 1. Selected Low-Level Laser Therapy Devices Cleared by the U.S. Food and Drug Administration

Device	Manufacturer	Date Cleared	510(k) No.	Indication
FX-635	Erchonia Corporation	6/01/2019	K190572	For adjunctive use in whole body musculoskeletal pain therapy
Super Pulsed Laser Technology	Multi Radiance Medical	01/13/2018	K171354	Providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin
Lightstream Low-Level Laser	SOLICA CORPORATION	04/03/2009	K081166	For adjunctive use in the temporary relief of pain associated with knee disorders with standard chiropractic practice
GRT LITE, MODEL 8-A	GRT SOLUTIONS, INC.	02/03/2006	K050668	Use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin
MICROLIGHT 830 LASER SYSTEM	MICROLIGHT CORPORATION OF AMERICA	02/06/2002	K010175	Use in pain therapy or related indication

A number of low-level lasers have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for the treatment of pain (Table 1). Data submitted for the MicroLight 830® Laser consisted of the application of the laser over the carpal tunnel 3 times a week for 5 weeks. The labeling states that the "MicroLight 830 Laser is indicated for adjunctive use in the temporary relief of hand and wrist pain associated with Carpal Tunnel Syndrome." In 2006, GRT LITE™ was cleared for marketing, listing the TUCO Erchonia PL3000, the Excalibur System, the MicroLight 830® Laser, and the Acculaser Pro as predicate devices. Indications of the GRT LITE for CTS are similar to the predicate devices: "adjunctive use in providing temporary relief of minor chronic pain." In 2009, the LightStream™ LLL device was cleared for marketing by the FDA through the 510(k) process for adjunctive use in the temporary relief of pain associated with knee disorders treated in standard chiropractic practice. A number of clinical trials of LLLT are underway in the U.S., including studies of wound healing. Since 2009, many more similar LLLT devices have received 510(k) clearance from the FDA.

POLICY

- A. Low-level laser therapy may be considered **medically necessary** for prevention of oral mucositis in individuals undergoing cancer treatment associated with increased risk of oral mucositis, including chemotherapy and/or radiotherapy, and/or hematopoietic cell transplantation (see Policy Guidelines).
- B. Low-level laser therapy is considered **experimental / investigational** for all other indications, including but not limited to:
 - 1. Carpal tunnel syndrome
 - 2. Neck pain
 - 3. Subacromial impingement
 - 4. Adhesive capsulitis
 - 5. Temporomandibular joint pain
 - 6. Low back pain
 - 7. Osteoarthritis knee pain
 - 8. Heel pain (i.e., Achilles tendinopathy, plantar fasciitis)
 - 9. Rheumatoid arthritis
 - 10. Bell palsy
 - 11. Fibromyalgia
 - 12. Wound healing
 - 13. Lymphedema

POLICY GUIDELINES

- A. In the meta-analysis of 18 trials comparing low-level laser therapy (LLLT) to chemotherapy or chemoradiation for prevention of oral mucositis (Oberoi et al [2014]), the course of LLLT was generally from day 0 through treatment. In studies of hematopoietic cell transplant, the course of LLLT began between day -7 and day 0 and continued as long as day 14 or 15. In studies that began LLLT at day -7 or day -5 before hematopoietic cell transplant, the course of laser therapy ended at day -1 or day 0.
- B. Other protocols have applied low-level laser energy to acupuncture points on the fingers and hand. This technique may be referred to as *laser acupuncture*. Laser acupuncture is not reviewed in this policy.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review has been updated regularly with a search of the PubMed database. The most recent literature update was performed through April 18, 2024.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition.

Validated outcome measures are necessary to ascertain whether a condition improves or worsens, and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

PREVENTION OF ORAL MUCOSITIS

Clinical Context and Therapy Purpose

The purpose of low-level laser therapy (LLLT) in individuals who have an increased risk of oral mucositis due to some cancer treatments and/or hematopoietic cell transplantation (HCT) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is those who have an increased risk of oral mucositis due to some cancer treatments and/or HCT. Oral mucositis is a common, painful complication of cancer treatments, particularly chemotherapy and radiation. It can lead to several problems, including pain, nutritional problems as a result of an inability to eat, and increased risk of infection due to open sores in the mucosa.

Interventions

The therapy being considered is LLLT, which can be used to treat oral mucositis. It is a non-invasive, simple, atraumatic therapeutic management corresponding to a local application of a high-density monochromatic narrow-band light source.

Comparators

Oral mucositis usually heals 2 to 4 weeks after the cessation of cytotoxic chemotherapy when no infection is present. Comparators of interest include general oral care protocols and medications, including topical anesthetics, antiseptics, and analgesics.

Outcomes

General outcomes of interest are reductions in symptoms, morbid events, and treatment-related morbidity and an improvement in the QOL. The effects of LLLT to promote healing are expected to occur from weeks to months. Outcomes can be measured using the Oral Mucositis Weekly Questionnaire-Head and Neck and the Functional Assessment of Cancer Treatment-Head and Neck Questionnaire.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE**Systematic Reviews**

In 2014, the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO) issued guidelines that reiterated findings from their 2012 systematic review recommending LLLT for the prevention of oral mucositis in patients receiving HCT conditioned with high-dose chemotherapy and for patients undergoing head and neck radiotherapy, without concomitant chemotherapy.¹ The 2014 systematic review included 24 trials on a variety of prophylactic treatments. Recommendations for the use of LLLT for prevention of oral mucositis in patients receiving HCT were based on what reviewers considered to be the well-designed, placebo-controlled, randomized trial by Schubert et al (2007),² together with "weaker evidence" from 3 observational studies that showed positive results. This phase 3 trial was double-blind and sham-controlled evaluating 70 patients.² Trial limitations included lack of statistically significant findings for the primary outcome measure and a very small percentage of patients with pain assessments. Overall, as it relates to the 3 observational studies, reviewers noted that, due to the range of laser devices and variations in individual protocols, results of each study applied exclusively to the cancer population studied and the specific wavelength and settings used.

Additional systematic reviews have been published since the MASCC/ISOO (2012) systematic review, with similar findings to support the use of LLLT.^{3,4,5} Oberoi et al (2014) reported on a systematic review and meta-analysis of 18 RCTs comparing LLLT with no treatment or placebo for oral mucositis in patients undergoing HCT.⁶ Eight RCTs assessed patients undergoing HCT, 8 evaluated head and neck cancer patients receiving radiotherapy or chemoradiation, and the rest studied patients with other conditions receiving chemotherapy. Reviewers used the Cochrane risk of bias tool to evaluate the RCTs. Most were considered at low-risk of bias on most domains. For

example, 68% were at low-risk of bias for blinding of patients and personnel, and 89% were at low-risk of bias on incomplete outcome data. The primary outcome measure for the review was the incidence of severe mucositis. Ten studies (N=689 patients) were included in a pooled analysis for this outcome. The overall incidence of severe mucositis (grades 3 to 4) decreased with prophylactic LLLT, with a relative risk (RR) of 0.37 (95% confidence interval [CI], 0.20 to 0.67; $p=.001$). Moreover, the absolute risk reduction in the incidence of severe mucositis (-0.35) significantly favored LLLT (95% CI, -0.48 to -0.21; $p<.001$). Among secondary outcomes, LLLT also significantly reduced the overall mean grade of mucositis (standardized mean difference [SMD], -1.49; 95% CI, -2.02 to -0.95), duration of severe mucositis (weighted mean difference [WMD], -5.32; 95% CI, -9.45 to -1.19), and incidence of severe pain as measured on a visual analog scale (VAS; relative risk, 0.26; 95% CI, 0.18 to 0.37). In a subgroup analysis of the primary outcome (incidence of severe mucositis), the investigators did not find a statistically significant interaction between the type of condition treated and the efficacy of LLLT.

Peng et al (2020) conducted a systematic review with meta-analysis comparing LLLT to placebo, usual care, or no therapy in patients receiving chemotherapy or radiotherapy for hematologic malignancies with or without HCT or head and neck squamous cell cancer (HNSCC).⁵ The systematic review included 30 studies including 1 with a stratified analysis. For the purposes of the meta-analysis, this was treated as an additional trial; 14 were conducted in Brazil and 10 were published between 2014 and 2018. Patients underwent HCT or chemotherapy in 19 studies; radiotherapy in 5 studies, and chemoradiotherapy in 6 studies. The application of LLLT was prophylactic in 26 studies and 6 studies reported on therapeutic LLLT use. Using the Jadad scale to assess for quality, 19 were considered high-quality (score of ≥ 3 out of 5 considered high quality). Ten trials were considered to be at low risk for bias. For use of prophylactic LLLT, a total of 22 studies (n=1190 patients) evaluated the incidence of the primary outcome of severe oral mucositis during the treatment of hematologic disorders or head and neck cancer. Severe oral mucositis occurred significantly less in patients receiving LLLT compared to control (RR, 0.40; 95% CI, 0.25 to 0.57; $p<.01$). This significant reduction in severe oral mucositis incidence with LLLT therapy was sustained in multiple subgroup analyses including by underlying condition/treatment regimen: HCT (RR, 0.46; 95% CI, 0.23 to 0.94; $p=.03$), chemotherapy (RR, 0.2; 95% CI, 0.05 to 0.92; $p=.04$), and radiotherapy (RR, 0.36; 95% CI, 0.27 to 0.50; $p<.01$). An analysis of 15 trials (n=900 patients) found that prophylactic LLLT numerically, but not significantly, reduced the incidence of oral mucositis of any grade (RR, 0.90; 95% CI, 0.98 to 1.00; $p=.06$). A subgroup analysis of patients receiving chemotherapy showed a significant reduction in any grade of mucositis with LLLT (RR, 0.73; 95% CI, 0.55 to 0.96; $p=.03$); this difference was not significant in patients receiving radiotherapy and chemoradiotherapy (RR, 1.00; 95% CI, 0.92 to 1.09; and RR, 1.00; 95% CI, 0.98 to 1.01, respectively).

Cruz et al (2023) conducted a systematic review and meta-analysis on the effects of LLLT on the treatment of oral mucositis in patient undergoing antineoplastic therapy.⁷ The systematic review included 6 studies, 5 RCTs and 1 single-arm study. For the meta-analysis, study participants were divided into an experimental group, receiving LLLT with or without other therapies, and a control group, who did not receive LLLT. Reduction in severity of oral mucositis was report in 5 studies, with a higher chance of reduction in the experimental group (5 studies; n=283; OR: 7.20; 95% CI, 2.88 to 17.98; I^2 , 31%). The authors conclude that LLLT could reduce oral mucositis severity. This meta-analysis has limitations including high heterogeneity and differences in protocols, methodologies, and treatment duration among the studies.

Franco et al (2023) conducted a systematic review and meta-analysis on LLLT for the treatment of oral mucositis induced by HCT.⁸ The review included 3 studies (N=98). There was a greater effect on mucositis severity in the treatment compared to control group (standard mean difference, -1.34; 95% CI, -1.98 to -0.69; I^2 , 38%; $p < .0001$).

Shen et al (2024) conducted a systematic review and meta-analysis of the efficacy of LLLT in 14 RCTs, searched between January 2000 and October 2023, treating oral mucositis in patients with head and neck cancer (N=869).⁹ From 2 weeks, the incidence of oral mucositis was significantly lower in the treatment compared to control group (6 studies; n=469; RR, 0.49; 95% CI, 0.25 to 0.97; I^2 , 71%; $p = .04$) through week 7 (5 studies; n=440; RR, 0.77; 95% CI, 0.61 to 0.99; I^2 , 89%; $p = .04$). From 3 weeks, the occurrence of severe mucositis was lower in the treatment compared to control group (5 studies; n=394; RR, 0.51; 95% CI, 0.29 to 0.90; I^2 , 12%; $p = .02$) until week 7 (5 studies; n=440; RR, 0.45; 95% CI, 0.24 to 0.85; I^2 , 80%; $p = .01$). Lack of standardization in treatment parameters and outcome measure tools are limitations of this meta-analysis.

Randomized Controlled Trials

Reyad et al (2023) published an RCT investigating LLLT to treat chemotherapy-induced oral mucositis in leukemic children (N=44).¹⁰ Patients were randomized 1:1 to treatment (n=22) or control (n=22) groups. The treatment group received LLLT in addition to symptomatic treatment and the control group received conventional symptomatic treatment. Primary outcomes were oral mucositis severity, measured by the WHO grading system, and discomfort and pain, measured using the VAS, and were reported at baseline, 5, 10, and 14 days after treatment. After 10 days, the treatment group had significantly improved oral mucositis severity grades ($p < .03$) and VAS scores ($p < .001$). At 14 days, the treatment group compared to the control group, had statistically significantly lower median (interquartile range [IQR]) oral mucositis severity grades (1.00 (1.00) vs. 2.00 (1.00); $p = .003$) and lower mean (standard deviation [SD]) VAS scores (1.27 (1.08) vs. 4.27 (2.71); $p < .001$). Compliance limits studies in children. Follow-up of treatment effects was limited to 14 days.

Section Summary: Prevention of Oral Mucositis

The literature on LLLT for the prevention of oral mucositis includes several systematic reviews, including a review by MASCC/ISOO (2012), with a resulting recommendation for LLLT for adults receiving HCT conditioned with high-dose chemotherapy and 1 RCT in leukemic children. The MASCC/ISOO recommendation for LLLT for preventing oral mucositis in patients undergoing radiotherapy for head and neck cancer was based on lower level evidence. Several systematic reviews have found benefit of LLLT, including a 2014 systematic review of LLLT for prevention of oral mucositis in patients undergoing HCT that included 18 RCTs, generally considered at low-risk of bias, and found statistically significantly better outcomes with LLLT than with control conditions on primary and secondary outcomes. A 2020 systematic review not limited to patients undergoing HCT showed benefit with using prophylactic LLLT compared to control in reducing the incidence of severe oral mucositis in patients undergoing chemotherapy or radiotherapy.

CARPAL TUNNEL SYNDROME

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals who have carpal tunnel syndrome (CTS) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with CTS, a common condition that causes pain, numbness, and tingling in the hand and arm. It is due to excess pressure in the wrist and on the median nerve, often caused by inflammation. Repeated motion of the wrist can contribute to the syndrome such as any repeated movement that overextends the wrist.

Women are more likely to have CTS than men, and it is frequently diagnosed between the ages of 30 and 60 years. Certain conditions can also increase the risk of developing CTS, including diabetes mellitus, high blood pressure, and arthritis.

Interventions

The therapy being considered is LLLT. Possible mechanisms of the benefits of LLLT include anti-inflammatory effects, selective inhibition of nociceptive activation at peripheral nerves, increased adenosine triphosphate (ATP) production and cellular respiration, and improvement of blood circulation to remove algogenic substances.

Comparators

The following practice is currently being used to treat CTS: conservative therapy (e.g., physical therapy, wrist splints) and medication for pain and inflammation. Surgery may also be performed, during which the transverse carpal ligament is cut often under local anesthetic.

Outcomes

The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months. Pain can be measured on a VAS score.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

A TEC Assessment (2010) evaluated LLLT for CTS and chronic neck pain. For inclusion in the Assessment, studies had to meet the following criteria: be published in a peer-reviewed journal, be a randomized, sham-controlled trial, and, if adjunctive therapies were used, they had to have been applied to both groups, and measure outcomes at least 2 weeks beyond the end of the treatment period. Four RCTs met the inclusion criteria. Reviewers concluded that the studies had

serious limitations, including small sample sizes and limited follow-up, and no study was so methodologically sound as to provide definitive results.

A 2016 Cochrane report assessed the benefits and harms of LLLT compared with placebo and compared with other non-surgical interventions in the management of CTS.¹¹ Twenty-two RCTs with 1153 participants were included. The authors concluded the quality of evidence was very low and found no data to support a clinical effect of LLLT in treating CTS.

Li et al (2016) published a meta-analysis of RCTs on LLLT for CTS.¹² Reviewers identified 7 RCTs. Meta-analyses evaluated outcomes for hand grip strength, pain measured by a VAS, symptom severity scores, and functional status scores. Short-term follow-up was defined as less than 6 weeks after treatment and long-term follow-up as at least 12 weeks after treatment. For 6 of the 8 meta-analyses, there were no statistically significant between-group differences in outcomes. They included short-term assessment of hand grip, short-term assessment of pain (VAS), and short- and long-term assessment of symptom severity and functional status scores. Meta-analyses found stronger hand grip (3 studies) and greater improvement in VAS scores (2 studies) at the long-term follow-up in the LLLT group than in the control. Most data for these 2 positive analyses were driven by a single RCT (Fusakul et al [2014]¹³). Reviewers concluded that additional high-quality trials with similar LLLT protocols would be needed to confirm that the intervention significantly improves health outcomes.

Section Summary: Carpal Tunnel Syndrome

A number of RCTs and several systematic reviews have been published. The most recent systematic review (2016) identified 7 RCTs. Meta-analyses did not find a significant benefit of LLLT compared with a control condition for most of the outcome measures (6 of 8). Previously, a TEC Assessment (2010) had concluded that the evidence from sham-controlled randomized trials was insufficient. More recent RCTs have not found that LLLT significantly improves outcomes.

NECK PAIN

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals who have neck pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with neck pain. Accompanying symptoms can include muscle tightness and spasms, decreased mobility, and headache. It can be caused by muscle strain, worn joints, nerve compression, injuries, or disease.

Interventions

The therapy being considered is LLLT, which uses laser irradiation to help repair tissue and relieve pain.

Comparators

The following practice is currently being used to treat neck pain: conservative therapy (e.g., physical therapy), medication, and surgery.

Outcomes

The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months. Pain can be measured on a VAS score.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE**Systematic review**

The TEC Assessment (2010), which included 6 trials of LLLT for chronic neck pain, found inconsistent results.¹⁴ In the largest study (Chow et al [2006]), 90 patients were randomized to active LLLT or sham treatment.¹⁵ Five weeks after the 7-week treatment period, patients in the active treatment group reported a 2.7-point improvement in VAS pain score versus 0.3-point worsening for the sham group. A calculated mean improvement of 43.8% was reported for the active LLLT group while the sham-treated group improved by 2.1%. The Assessment noted that baseline VAS pain scores were significantly higher in the active treatment group, possibly biasing results in favor of LLLT. Overall, reviewers concluded that the trials were characterized by small sample sizes, limited statistical power, and limited long-term follow-up, and thus the evidence was insufficient.

In a systematic review and meta-regression, Gross et al (2013) evaluated 17 trials on LLLT for neck pain.¹⁶ Ten trials demonstrated a high-risk of bias. Two trials (n=109 subjects) were considered of moderate quality and found LLLT produced better outcomes than placebo for chronic neck pain treatment. Other trials showed improved outcomes with LLLT compared with placebo for acute neck pain, acute radiculopathy, and cervical osteoarthritis, but they were considered to be low-quality. There was conflicting evidence on chronic myofascial neck pain.

Section Summary: Neck Pain

A number of RCTs and several systematic reviews have been published. A 2013 systematic review identified 17 trials. Only 2 trials considered of moderate quality found that LLLT led to better outcomes than placebo for chronic neck pain. Other trials were considered low-quality. A 2010 TEC Assessment found conflicting evidence. While some studies showed positive benefits with LLLT over placebo, others did not. Additionally, laser types, dosages, and treatment schedules varied in the available evidence.

SUBACROMIAL IMPINGEMENT SYNDROME

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals with subacromial impingement syndrome is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with subacromial impingement syndrome, involving tendonitis of the rotator cuff muscles as they pass through the subacromial space. It can result in pain, weakness, and loss of movement at the shoulder.

Interventions

The therapy being considered is LLLT.

Comparators

The following practice is currently being used to treat subacromial impingement syndrome: conservative therapy (e.g., physical therapy, rest, cessation of painful activity), medication (such as corticosteroids and local anesthetics), and surgery. Surgery can be done arthroscopically or as open surgery.

Outcomes

The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months. Pain can be measured on a VAS score and on the Shoulder Pain and Disability Index (SPADI).

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE**Randomized Controlled Trials**

Several RCTs evaluating LLLT for the treatment of subacromial impingement syndrome have been published. Two sham-controlled studies, by Yeldan et al (2009)¹⁷, and by Dogan et al (2010)¹⁸, did not find statistically significantly better pain or functional outcomes with active treatment than with sham. A third RCT, by Abrisham et al (2011), compared exercise plus pulsed LLLT with sham laser 5 times a week for 2 weeks in 80 patients who had a subacromial syndrome (rotator cuff and biceps tendinitis).¹⁹ At the end of treatment, while both groups had improved VAS scores for pain and shoulder range of motion (ROM), the improvements were significantly better for the active LLLT group than for the sham laser group for pain (VAS score,

4.4 vs. 2.9) and all measures of ROM (active and passive flexion, abduction, external rotation). The durability of this effect was not assessed.

Other RCTs have not shown statistically significant benefits of LLLT versus conservative treatment. In a study designed to assess the effectiveness of LLLT in patients with subacromial impingement syndrome, Bal et al (2009) randomized 44 patients to a 12-week home exercise program with or without LLLT.²⁰ Outcome measures of night pain, SPADI, and University of California-Los Angeles shoulder pain end-result scores were assessed at weeks 2 and 12 of the intervention. No distinct advantage was demonstrated by LLLT over exercise alone. Both groups showed significant reductions in night pain and SPADI scores at 2- and 12-week assessments, but the differences between groups were not statistically significant.

Calis et al (2011) randomized 52 patients with subacromial impingement syndrome to LLLT, ultrasound, or exercise.²¹ Patients were treated 5 days a week for 3 weeks with hot pack plus ultrasound plus exercise, hot pack plus LLLT plus exercise, or hot pack plus exercise. All 3 groups showed improvements from baseline to posttreatment in pain at rest, ROM, and function, but between-group improvements with LLLT were not statistically significant.

Alfredo et al (2020) randomized 122 patients to LLLT plus exercise (n=44; 42 included in analysis), LLLT alone (n=42), or exercise alone (n=42) for 8 weeks.²² Therapy was given 3 times a week for 8 weeks. Between-group comparison showed that patients in the LLLT plus exercise group had a significantly greater improvement in SPADI compared to other groups; however, no between-group comparison was performed exclusively for patients receiving LLLT alone and exercise alone.

Badil Güloğlu (2021) randomized 64 patients with a recent diagnosis of subacromial impingement syndrome without treatment in the preceding 4 weeks to 15 sessions of LLLT (n=34) every weekday for 3 weeks or to weekly sessions of extracorporeal shock wave treatment (ESWT; n=30) for 3 weeks.²³ In both groups, all range of motion measurements, visual analogue scale pain scores, and SPADI scores showed significant improvements both at the end of treatment and at the third month after treatment ($p < .05$). There was no significant difference in abduction between the groups except the change at the end of treatment ($p > .05$). The ESWT group showed greater improvements in terms of SPADI disability and total scores at the end of treatment compared to LLLT. The improvements in VAS pain scores and SPADI scores at the third month after treatment was significantly more evident in the ESWT group ($p < .05$). Tables 2 and 3 provide RCT characteristics and results for evaluation of treatment of subacromial impingement syndrome.

Table 2. Summary of Key Randomized Controlled Trial Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Yeldan et al (2009) ¹⁷	Turkey	1	NR	Patients with SAIS	LLLT (n=34)	Placebo (n=33)
Bal et al (2009) ²⁰	Turkey	1	NR	Newly-diagnosed SAIS patients	LLLT + 12-wk home exercise program (n=22)	12-wk home exercise program (n=22)

Study	Countries	Sites	Dates	Participants	Interventions	
Dogan et al (2010) ¹⁸ ,	Turkey	NR	NR	Patients with SAIS	LLLT (n=30)	Placebo (n=22)
Abrisham et al (2011) ¹⁹ ,	Iran	1	NR	Patients with SAIS (rotator cuff and biceps tendinitis)	LLLT (n=40)	Placebo (n=40)
Calis et al (2011) ²¹ ,	Turkey	NR	NR	Patients with SAIS	LLLT + moist heat + exercise (n=15)	Comparator 1: Moist heat + ultrasound + exercise (n=21) Comparator 2: Moist heat + exercise (n=16)
Alfredo et al (2020) ²² ,	Brazil	1	2015-2016	Patients with SAIS, aged 50 to 70 years	LLLT + exercise (n=42); LLLT alone (n=36)	Exercise only (n=42)
Badil Güloğlu (2021) ²³ ,	Turkey	1	2019	Patients with newly diagnosed SAIS, aged 18 to 65 years	LLLT (n=34)	ESWT (n=30)

ESWT: extracorporeal shock wave therapy; LLLT: low-level laser therapy; NR: not reported; SAIS: subacromial impingement syndrome.

Table 3. Summary of Key Randomized Controlled Trial Results

Study	Pain	ROM (°)
Yeldan et al (2009) ¹⁷ ,	VAS-A; VAS-R; VAS-N (Change from Baseline)	NR
LLLT	-2.20 ± 1.78; -1.47 ± 2.12; -2.85 ± 1.98	
Placebo	-2.15 ± 2.11; -2.03 ± 2.45; -3.07 ± 2.81	
p -value	.94;.30;.79	
Bal et al (2009) ²⁰ ,	SPADI (Change from Baseline)	NR
LLLT	-37 ± 18.58	
Exercise	-37.2 ± 21.28	
p-value	.486	
Dogan et al (2010) ¹⁸ ,	VAS (Baseline; Posttreatment)	NR
LLLT	7.16 ± 1.64; 3.76 ± 1.45	
Placebo	7.59 ± 1.76; 4.63 ± 2.10	
p-value	.343;.216	
Abrisham et al (2011) ¹⁹ ,	VAS (Post treatment)	Active Flexion, mean

Study	Pain	ROM (°)
LLLT	4.4±1.2	43.1±2.5
Placebo	2.9±1.1	25.3±2.4
p-value	.000	.000
Calis et al (2011) ²¹ ,	VAS at Rest (Baseline; Post treatment)	Flexion (Baseline; Post-treatment)
LLLT	4.00±3.45; 2.56±2.28	163.80±10.05; 174.46±6.94
Ultrasound	3.56±2.49; 2.21±2.09	168.33±1.34; 177.04±3.74
Control	4.67±2.47; 3.96±2.71	163.06±8.57; 172.18±6.93
p-value	.49; .10	.21; .05
Alfredo et al (2020) ²² ,	SPADI (Posttreatment value [median quartile])	Flexion (Baseline; Posttreatment)
LLLT + exercise	0 (0 to 10)	132.9±27.1; 161.5±10.9
LLLT	16 (10.0 to 27.5)	124.9±35.0; 153.5±17.9
Exercise	41 (8.0 to 86.0)	118.4±28.1; 137.1±24.1
p-value	<.001	<.001
Badil Güloğlu (2021) ²³ ,	SPADI (End of treatment; Third month after treatment)	Change in Abduction (Before treatment to end of treatment difference)
LLLT	48 (range, 12 to 92); 52 (range, 12 to 80)	-10 to 100; median, 30
ESWT	35 (range, 0 to 76); 32 (range, 0 to 68)	0 to 50; median, 20
p-value	.003; .002	.018

ESWT: extracorporeal shock wave therapy; LLLT: low level laser therapy; ROM: range of motion; SPADI: shoulder pain and disability index; VAS: visual analog scale; VAS-A: visual analog scale-activity; VAS-N: visual analog scale-night; VAS-R: visual analog scale-rest.

Tables 4 and 5 display notable limitations identified in each study.

Table 4. Subacromial Impingement Syndrome Randomized Controlled Trial Study Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Follow-Up ^e
Yeldan et al (2009) ¹⁷ ,	3,4. 78.3% of patients included in the analysis were female				1,2. Follow-up duration limited to 3 weeks

Study	Population^a	Intervention^b	Comparator^c	Outcomes^d	Follow-Up^e
Bal et al (2009) ²⁰ ,	3,4. 70% of patients included in the analysis were female				
Dogan et al (2010) ¹⁸ ,					1,2. Follow-up duration not specified
Abrisham et al (2011) ¹⁹ ,					1,2. Follow-up duration limited to 3 weeks
Calis et al (2011) ²¹ ,					
Alfredo et al (2020) ²² ,	2. Detailed baseline characteristics (e.g., gender) not presented				
Badil Güloğlu (2021) ²³ ,	3,4. 70.6%, of patients in the LLLT group were female		2,3. ESWT efficacy not completely established.		

ESWT: extracorporeal shock wave treatment; LLLT: low-level laser therapy.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

^a Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.

^b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5. Other.

^c Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

^d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.

^e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 5. Subacromial Impingement Syndrome Randomized Controlled Trial Study Design and Conduct Limitations

Study	Allocation^a	Blinding^b	Selective Reporting^c	Follow-Up^d	Power^e	Statistical^f
Yeldan et al (2009) ¹⁷ ,	2. Allocation not concealed	2. Blinding unclear				
Bal et al (2009) ²⁰ ,	3. Allocation concealment unclear	1,2,3. Blinding unclear				
Dogan et al (2010) ¹⁸ ,	3. Allocation concealment unclear					
Abrisham et al (2011) ¹⁹ ,	3. Allocation concealment unclear	1,2,3. Blinding not described				
Calis et al (2011) ²¹ ,	3. Allocation concealment unclear	1,2,3. Not blinded				
Alfredo et al (2020) ²² ,		1,2,3. Not blinded		6. Per protocol analysis performed; however, only 2 patients were excluded from this analysis		4. No comparative analysis performed to compare LLLT only group with exercise only group
Badil Güloğlu (2021) ²³ ,		1,2,3. Not blinded		6. Per protocol analysis performed (7 patients excluded from analysis)		

LLLT: low-level laser therapy.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

^a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

^b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

^c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

^d Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

^e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

^f Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Subacromial Impingement Syndrome

The literature on LLLT for subacromial impingement syndrome consists of several RCTs. Most trials failed to show a significant benefit of LLLT compared with sham treatments or alternative interventions (e.g., exercise).

ADHESIVE CAPSULITIS**Clinical Context and Therapy Purpose**

The purpose of LLLT in individuals with adhesive capsulitis is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with adhesive capsulitis, also known as frozen shoulder. In this condition, the connective tissue surrounding the glenohumeral joint, becoming inflamed, stiff, and painful.

Risk factors for adhesive capsulitis include tonic seizures, diabetes mellitus, stroke, and lung, heart, and thyroid diseases. It occurs most frequently in women aged 40 to 65 years.

Interventions

The therapy being considered is LLLT.

Comparators

The following practice is currently being used to treat adhesive capsulitis: conservative therapy (e.g., physical therapy), medication, and surgery.

Outcomes

The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months. Outcomes can be measured using the SPADI and the Croft Shoulder Disability Questionnaire.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Review

A Cochrane review by Page et al (2014) evaluated LLLT and other electrotherapy modalities for adhesive capsulitis (ie, frozen shoulder).²⁴ Reviewers found limited evidence on which to conclude whether electrotherapy modalities are effective for frozen shoulder. Only 1 RCT (N=40 patients) compared LLLT with placebo. That trial administered LLLT for 6 days. On day 6, patients receiving LLLT showed some improvements on a global assessment of treatment success compared with patients receiving a placebo. However, this trial was considered low-quality, and its small sample size and short follow-up limited interpretation of results. Another RCT on LLLT discussed in the 2014 Cochrane review was assessed as moderate quality. In that RCT, Stergioulas et al (2008) randomized 63 patients with frozen shoulder to an 8-week program of LLLT (n=31) or placebo (n=32).²⁵ Both groups also participated in exercise therapy. Compared with the sham group, the active laser group had a significant decrease in overall, night, and activity pain scores after 4 and 8 weeks of treatment and at the end of 8 more weeks of follow-up. At the same assessment intervals, significant decreases in SPADI and Croft Shoulder Disability Questionnaire scores were observed, while significant decreases in Disability of Arm, Shoulder, and Hand Questionnaire scores were observed at 8 weeks of treatment and 16 weeks post-randomization; significant decreases in Health Assessment Questionnaire scores were observed at 4 weeks and 8 weeks of treatment.

Section Summary: Adhesive Capsulitis

A Cochrane review evaluating treatments for adhesive capsulitis identified 2 RCTs on LLLT for adhesive capsulitis and, due to the small number of trials and study limitations, concluded that the evidence was insufficient to conclude whether LLLT is effective for adhesive capsulitis.

TEMPOROMANDIBULAR JOINT PAIN

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals who have temporomandibular joint (TMJ) pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with TMJ pain.

Interventions

The therapy being considered is LLLT.

Comparators

The following practice is currently being used to treat TMJ pain: conservative therapy (e.g., physical therapy), medication, and surgery.

Outcomes

The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

Several meta-analyses of RCTs on LLLT for TMJ pain have been published. A meta-analysis by Chen et al (2015) assessed pain and functional outcomes after LLLT for TMJ pain.²⁶ Fourteen placebo-controlled randomized trials were identified. Ten trials provided data on pain, as measured by a VAS. Pooled analysis of these studies found no significant differences between active treatment and placebo for VAS scores at final follow-up (WMD, -19.39; 95% CI, -40.80 to 2.03; $p=.08$). However, meta-analyses did find significantly better functional outcomes (ie, maximum active mouth opening, maximum passive mouth opening) favoring LLLT. For example, the mean difference (MD) in maximum active mouth opening for active treatment versus placebo was 4.18 (95% CI, 0.73 to 7.63).

Chang et al (2014) published a meta-analysis of 7 RCTs on LLLT for TMJ pain.²⁷ Single- or double-blind RCTs included in the review compared LLLT with no treatment or placebo. The primary outcome of interest was pain measured by a VAS. Six studies (N=223 patients) were eligible for inclusion in the meta-analysis. In a meta-analysis, reduction in VAS scores after treatment was significantly greater in the LLLT group than in the control group (pooled effect size, -0.6; 95% CI, -0.47 to -0.73).

Hanna et al (2021) recently published the largest systematic review including 44 RCTs of LLLT for TMJ pain to date.²⁸ All included trials were at low risk for reporting missing outcome data. Seventy percent of the included trials were at low risk, 28% were at high risk, and 2% had some concerns in terms of reporting outcome measurement. Of the RCTs included, 98% were at low risk of bias for selective reporting of the results. Overall, 38% of studies reported a low risk of bias, 46% were at high risk, and 16% had some concerns. Comparators across RCTs included sham placebo, drug therapy and physiotherapy. The primary outcome of interest was change in pain intensity reduction from baseline, measured by a VAS. Thirty-three studies (n=1163) were eligible for inclusion in the meta-analysis. In a meta-analysis, pooled change in VAS score from baseline to final follow-up evaluation demonstrated a significantly greater reduction with LLLT compared to comparator groups (pooled SMD, -0.55; 95% CI, -0.82 to -0.27; $p<.0001$), however, heterogeneity was high ($I^2=78\%$).

Zhang et al (2023) published a systematic review and meta-analysis of laser therapy on temporomandibular disorders, including 28 RCTs.²⁹ Overall, laser therapy had a statistically significant effect on VAS (21 studies; n=934; SMD: -1.88; 95% CI, -2.46 to -1.30; $p<.00001$; I^2 , 93%), maximum active vertical opening (17 studies; n=732; MD, 4.90; 95% CI, 3.29 to 6.50; $p<.00001$; I^2 , 72%), maximum passive vertical opening (5 studies; n=300; MD, 5.82; 95% CI,

4.62 to 7.01; $p < .00001$; I^2 , 40%), and right lateral movement (6 studies; $n=261$; MD, 0.73; 95% CI, 0.23 to 1.22; $p = .004$; I^2 , 0%). The authors note that while the results demonstrated effective pain relief, there was variation among the included studies, including various laser parameter settings. RCTs with larger sample sizes are needed for higher quality evidence.

Arribas-Pascual et al (2023) published systematic review and meta-analysis on the effects of various physiotherapy interventions on pain and mouth opening in temporomandibular disorders.³⁰ They conducted a sub-analysis on 4 studies of LLLT. They found a statistically significant effect of LLLT on pain intensity (SMD, 0.8; 95% CI, 1.44 to 0.17; $p < .001$; I^2 , 27%) and maximum mouth opening (SMD, 0.95; 95% CI, 1.5 to 0.39; $p < .001$; I^2 , 21%). The overall confidence of studies included in the systematic review were low or critically low. The systematic review did not adequately report sample sizes among the studies used in the LLLT sub-analyses. Overall, the results are of a low quality of evidence.

Tables 6 through 8 provide further details of these systematic reviews.

Table 6. Comparison of Trials/Studies Included in Systematic Reviews & Meta-Analysis

Study	Chen et al (2015) ²⁶ ,	Chang et al (2014) ²⁷ ,	Hanna et al (2021) ²⁸ ,	Zhang et al (2023) ^{29,a}
Conti et al (1997) ³¹ ,	●			
Kulekcioglu et al (2003) ³² ,	●			
Venancio et al (2005) ³³ ,	●	●	●	●
Cetiner et al (2006) ³⁴ ,		●	●	●
Fikackova et al (2007) ³⁵ ,		●	●	
Mazzetto et al (2007) ³⁶ ,	●	●	●	
Frare et al (2008) ³⁷ ,			●	
da Cunha et al (2008) ³⁸ ,	●	●	●	●
Lassemi et al (2008) ³⁹ ,			●	
Carrasco et al (2008) ⁴⁰ ,	●	●	●	
Emshoff et al (2008) ⁴¹ ,	●	●	●	
Carrasco et al (2009) ⁴² ,			●	
Shirani et al (2009) ⁴³ ,	●		●	●
Venezian et al (2010) ⁴⁴ ,			●	
Oz et al (2010) ⁴⁵ ,			●	
Marini et al (2010) ⁴⁶ ,	●		●	●
Santos et al (2010) ⁴⁷ ,				●
Rohlig et al (2011) ⁴⁸ ,			●	

Study	Chen et al (2015)^{26,}	Chang et al (2014)^{27,}	Hanna et al (2021)^{28,}	Zhang et al (2023)^{29,a}
Wang et al (2011) ^{49,}				●
Sattayut et al (2012) ^{50,}	●		●	
de Carli et al (2012) ^{51,}			●	
da Silva et al (2012) ^{52,}	●		●	●
Panhoca et al (2013) ^{53,}			●	
Uemoto et al (2013) ^{54,}			●	
Ferreira et al (2013) ^{55,}	●			
Demirkol et al (2014) ^{56,}	●			●
Ahrari et al (2014) ^{57,}	●		●	●
Pereira et al (2014) ^{58,}			●	
Maia et al (2014) ^{59,}			●	
Fornaini et al (2015) ^{60,}				●
Sancakli et al (2015) ^{61,}			●	●
De Oliveira et al (2017) ^{62,}			●	
Costa et al (2017) ^{63,}			●	●
Seifi et al (2017) ^{64,}			●	●
Shobha et al (2017) ^{65,}			●	●
Rezazadeh et al (2017) ^{66,}			●	
Varma et al (2018) ^{67,}			●	
Borges et al (2018) ^{68,}			●	
Brochado et al (2018) ^{69,}			●	
Rodrigues et al (2018) ^{70,}			●	
Peimani et al (2018) ^{71,}			●	
Nadershah et al (2019) ^{72,}			●	
Magri et al (2019) ^{73,}			●	
Al-Quisi et al (2019) ^{74,}			●	
Herpich et al (2019) ^{75,}			●	
Khairnar et al (2019) ^{76,}			●	
Madani et al (2020) ^{77,}				●
Sobral et al (2020) ^{78,}			●	

Study	Chen et al (2015)^{26,}	Chang et al (2014)^{27,}	Hanna et al (2021)^{28,}	Zhang et al (2023)^{29,a}
Maracci et al (2022) ^{79,}			●	
Chellappa et al (2020) ^{80,}			●	
Monteiro et al (2020) ^{81,}			●	
Del Vecchio et al (2021) ^{82,}				●
Shousha et al (2021) ^{83,}				●
Yamaner et al (2022) ^{84,}				●
Ekici et al (2022) ^{85,}				●
Ekici et al (2022) ^{86,}				●
Ekici et al (2022) ^{87,}				●

a. Three studies from this meta-analysis are not included in the table due to lack of availability in PubMed.

Table 7. Systematic Reviews & Meta-Analysis Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Chen et al (2015) ^{26,}	2003-2014	14	Patients suffering from TMDs	454 (NR)	RCT	NR
Chang et al (2014) ^{27,}	2006-2008	7	Patients suffering from TMDs	NR (NR)	RCT	NR
Hanna et al (2021) ^{28,}	2005-2021	44	Patients with TMDs	1163 (10 to >50)	RCT	4 days to 8 weeks
Zhang et al (2023) ^{29,}	2005-2022	28	Patients with TMDs	1121 (16 to 75)	RCT	NR

NR: not reported; RCT: randomized controlled trial; TMD: temporomandibular disorders.

Table 8. Systematic Reviews & Meta-Analysis Results

Study	Pain (VAS)	MAVO	MPVO
Chen et al (2015) ^{26,}			
WMD	-19.39	4.18	6.73
95% CI	-40.80 to 2.03	0.73 to 7.63	1.34 to 12.13
p -value	<.001	.006	.06
Chang et al (2014) ^{27,}			
ES (95% CI)	-0.60 (-0.47 to -0.73)	NR	NR
Hanna et al (2021) ^{28,}			
SMD (95% CI)	-0.55 (-0.83 to -0.28)	-0.40 (-0.61 to -0.20)	NR

Study	Pain (VAS)	MAVO	MPVO
p -value	<.0001	.0001	
I^2 (p)	78% (<.0001)	0% (.56)	
Zhang et al (2023) ²⁹ ,			
SMD (95% CI)	-1.88 (-2.46 to -1.30)	NA	NA
MD (95% CI)	NA	4.90 (3.29 to 6.50)	5.82 (4.62 to 7.01)
p-value	.00001	.00001	.00001
I^2	93%	72%	40%

CI: confidence interval; ES: effect size; MAVO: maximum active vertical opening; MD: mean difference; MPVO: maximum passive vertical opening; NA: not applicable; NR: not reported; SMD: standard mean difference; VAS: visual analog scale; WMD: weighted mean difference.

Randomized Controlled Trials

Several RCTs have been published since the meta-analyses, showing inconsistent results.

Del Vecchio et al (2021) randomized 90 patients between the ages of 18 and 73 years old with TMJ disorders to home LLLT (808 nm, 5 J/min, 250 mW, 15 KHz for 8 minutes twice daily), sham control, or standard conventional drugs (nimesulide 100 mg daily with 5-days of cyclobenzaprine 10 mg daily) for 1 week.⁸² Pain was measured using a 100-mm VAS, and the examiner was blinded. At the end of treatment, the reduction in VAS was greater in the LLLT group (MD, 13.030; $p=.036$) and the drug group (MD, 14.409; $p=.17$) compared to the sham group. However, no significant difference in pain reduction was observed between the LLLT group and the drug group (MD, 1.379; $p=1$). This study evaluated a specific at-home LLLT protocol and can not be generalized to other LLLT regimens.

Aisaiti et al (2021) randomized 78 patients with TMJ pain to receive LLLT (810 nm, 6 J/cm², applied at 5 points for 30 seconds) or placebo once daily for 7 consecutive days.⁸⁸ Pain was measured on a 0 to 10 numerical rating scale and pressure pain thresholds. Only 50 patients, 25 per group, remained in the study to contribute data to analysis. Greater reduction in numerical rating scale pain scores were seen with LLLT than with placebo ($p=.014$), but no significant interaction between time and intervention was found ($p=.35$). For pressure pain thresholds, there was no significant difference found between interventions or interaction between time and intervention.

Desai et al (2022) randomized 60 patients with TMJ disorders to LLLT or placebo given for 20 sessions over 8 weeks.⁸⁹ By week 8 both the placebo group and LLLT group had improvements from baseline with a final mean VAS of 5.2 in the placebo group and 3.2 in the LLLT group. There was no statistical comparison reported between groups. Mouth opening and lateral movement were also improved in both groups compared to baseline; however, improvements were numerically greater in the LLLT group. The small sample size, single-center design, and lack of comparison between active and placebo treatment limit generalizability of these findings.

Chamani et al (2024) randomized 42 patients with temporomandibular disorders into 3 groups: LLLT (n=14), placebo (n=15), or standard treatment (n=13).⁹⁰ The LLLT group received treatment 2 times per week for 10 sessions. All groups showed a statistically significant improvement in VAS ($p=.0001$), lateral jaw movements ($p=.0001$) forward jaw movement ($p=.007$), but not in maximum mouth opening. There was no significant difference between groups. The authors conclude that LLLT may be effective in treating temporomandibular disorders, but there was no difference to standard therapy. This study is limited by its small sample size and single-center design, so further evidence is needed.

Section Summary: Temporomandibular Joint Pain

A number of RCTs and several systematic reviews have evaluated LLLT for TMJ pain. Meta-analyses of these trials had mixed findings. The largest and most recent meta-analysis, using 33 randomized trials, found a statistically significant impact of LLLT on pain reduction and functional outcomes (e.g., mouth opening) compared to sham laser or other therapies including drug therapy; however heterogeneity was high amongst included trials. Randomized controlled trials have not compared the impact of LLLT with physical therapy on health outcomes.

LOW BACK PAIN

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals with low back pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with low back pain. It can be the result of an injury, such as muscle strains, or disease.

Interventions

The therapy being considered is LLLT.

Comparators

The following practices are currently being used to treat low back pain: conservative therapy (e.g., physical therapy), medication, and surgery. These medications can include muscle relaxants and nonsteroidal anti-inflammatory drugs.

Outcomes

The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

A number of RCTs and several systematic reviews of RCTs have assessed LLLT for low back pain. For example, Glazov et al (2016) published a meta-analysis of blinded sham-controlled trials evaluating LLLT for treatment of chronic low back pain.⁹¹ Fifteen RCTs (N=1039 patients) met reviewers' eligibility criteria. Reviewers found that 3 of the 15 trials were at higher risk of bias (using a modified Cochrane risk of bias tool), mainly due to lack of blinding. The primary outcomes of interest to reviewers were pain measured by a VAS or a numeric rating scale, and a global assessment measure evaluating overall improvement and/or satisfaction with the intervention. Outcomes were reported immediately posttreatment (<1 week) and at short-term (1 to 12 weeks) follow-up. Longer-term outcomes (ie, at 6 and 12 months) were secondary measures. For the pain outcomes, a meta-analysis of 10 trials found a significantly greater reduction in pain scores in the LLLT group at immediate follow-up (WMD, -0.79 cm; 95% CI, -1.22 to 0.36 cm). In a meta-analysis of 6 trials, there was no significant difference in pain reduction at short-term follow-up. However, in subgroup analyses, there was a significantly greater reduction in pain with LLLT in trials that used a higher dose (>3 J/point), but not a lower dose, and in trials that included patients with a short duration of back pain (5 to 27 months) but not long duration (49 months to 13 years). Decisions on the cutoff to use for laser dose and duration of back pain were made post hoc and considered review findings. Findings were similar for the global assessment outcome. Meta-analyses found significantly higher global assessment scores at immediate follow-up (5 trials) but not at short-term follow-up (3 trials). Only 2 trials reported pain or global assessment at 6 and 12 months, and neither found statistically significant differences between the LLLT and sham groups.

Huang et al (2015) published a systematic review of RCTs on LLLT for treating nonspecific chronic low back pain.⁹² Reviewers included trials comparing LLLT with placebo that reported pain and/or functional outcomes and a Physiotherapy Evidence Database (PEDro) quality score. Seven trials (N=394 patients; 202 assigned to LLLT, 192 assigned to placebo) were included. Six of the 7 trials were considered high-quality (ie, a PEDro score ³⁷; maximum score, 11 points). Primary outcomes of interest were posttreatment pain measured by VAS score and disability measured by the Oswestry Disability Index (ODI) score. Change in pain and ROM scores were secondary outcomes. In pooled analyses, reviewers found a statistically significant benefit of LLLT on pain outcomes but not disability or ROM. For the primary outcome (posttreatment pain scores) in a meta-analysis of all 7 trials, mean VAS scores were significantly lower in the LLLT group than in the placebo group (WMD, -13.57; 95% CI, -17.42 to -9.72). In a meta-analysis of 4 studies reporting the other primary outcome (ODI score), there was no statistically significant difference between the LLLT and the placebo groups (WMD, -2.89; 95% CI, -7.88 to 2.29). Outcomes were only reported immediately after treatment.

Chen et al (2022) published a systematic review of RCTs on LLLT for treating nonspecific chronic low back pain compared to placebo.⁹³ Eleven trials were included that compared LLLT to placebo (N=836 patients); 7 of these trials assessed LLLT alone compared to placebo and 4 trials assessed LLLT plus acupuncture compared to placebo. For the overall risk of bias in LLLT trials, 8

were identified as low risk, 2 as having some concerns, and 1 as high risk. The primary outcomes of interest were changes from baseline in pain scores, measured by VAS, and disability measured by the ODI score. In pooled analyses, reviewers found a significant reduction in pain scores with all LLLT interventions compared to placebo posttreatment (SMD, -0.22; 95% CI, -0.38 to -0.05) and in disability scores for trials comparing LLLT therapy alone compared to placebo (SMD, -0.50; 95% CI, -0.79 to -0.21). In trials comparing LLLT plus acupuncture to placebo, there was no significant difference in disability scores posttreatment (SMD, 0.10; 95% CI, -0.15 to 0.35).

Table 9 to 11 summarize meta-analyses for LLLT in low back pain.

Table 9. Comparison of Trials/Studies Included in Systematic Reviews & Meta-Analysis for Low Back Pain

Study	Glazov et al (2016) ^{91,}	Huang et al (2015) ^{92,}	Chen et al (2022) ^{93,}
Alayat et al (2014) ^{94,}	●		
Ay et al (2010) ^{95,}	●		●
Basford et al (1999) ^{96,}	●	●	●
Djavid et al (2007) ^{97,}	●	●	●
Glazov et al (2009) ^{98,}	●		●
Glazov et al (2014) ^{99,}	●		●
Klein et al (1990) ^{100,}	●	●	
Konstantinovic et al (2011) ^{101,}	●		
Lin et al (2012) ^{102,}	●		●
Okamoto et al (1989) ^{103,}	●		
Ruth et al (2010) ^{104,}	●		
Soriano et al (1998) ^{105,}	●	●	
Umegaki et al (1989) ^{106,}	●		
Vallone et al (2014) ^{107,}	●	●	
Wallace et al (1996) ^{108,}	●		
Gur et al (2003) ^{109,}		●	●
Hsieh et al (2014) ^{110,}		●	
de Carvalho et al (2016) ^{111,}			●
Tantawy et al (2019) ^{112,}			●
Nambi et al (2018) ^{113,}			●
Shin et al (2015) ^{114,}			●

Table 10. Systematic Reviews & Meta-Analysis Characteristics for Low Back Pain

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Glazov et al (2016) ⁹¹ ,	1989-2014	15	Non-pregnant adults with CLBP	1039 (20-144)	RCT	NR
Huang et al (2015) ⁹² ,	1990-2014	7	Patients with nonspecific CLBP	394 (20-100)	RCT	NR
Chen et al (2022) ⁹³ ,	1999-2020	11	Patients with nonspecific CLBP	836 (30-220)	RCT	NR

CLBP: chronic low back pain; NR: not reported; RCT: randomized controlled trial.

Table 11. Systematic Reviews & Meta-Analysis Results for Low Back Pain

Study	Pain	Disability Score
Glazov et al (2016) ⁹¹ ,	VAS (LLLT vs. Control)	NR
WMD	-0.79	
95% CI	-1.22 to -0.36	
I^2	70%	
Huang et al (2015) ⁹² ,	VAS (LLLT vs. Control)	ODI (LLLT vs. Control)
WMD	-13.57	-2.89
95% CI	-17.42 to -9.72	-7.88 to 2.29
I^2	0%	88%
Chen et al (2022) ⁹³ ,	VAS (LLLT + acupuncture vs. Control)	ODI (LLLT vs. Control; LLLT + acupuncture vs. Control)
SMD	-0.22	-0.50; 0.10
95% CI	-0.38 to -0.05	-0.79 to -0.21; -0.15 to 0.35
p -value	.009	.0007;.44
I^2	24%	11%; 0%

CI: confidence interval; LLLT: low-level laser therapy; NR: not reported; ODI: Oswestry Disability Index; SMD: standard mean difference; VAS: visual analog scale; WMD: weighted mean difference.

Randomized Controlled Trials

In a double-blind RCT, Koldas Dogan et al (2017) compared the effectiveness of 2 laser therapy regimens on pain, lumbar ROM, and functional capacity in patients with chronic low back pain.¹¹⁵ This trial assessed 49 patients with chronic low back pain who were randomized to a hot pack and the 2 different laser therapies for a total of 15 sessions. A series of assessments were conducted before and after treatment, including a modified Schober test, right and left lateral flexion measurements, VAS, and a modified ODI. After treatment, both groups saw a significant improvement in VAS, ODI, and lumbar ROM ($p < .05$). However, group 2 saw significantly better results in lateral flexion measurements and ODI scores ($p < .05$). Trial limitations included: (1) the short duration of follow-up; and (2) use of hot packs, which might have biased the pain

measurements. No superiority was found for 1 laser treatment over the other regarding pain relief; however, regarding functionality, patients might find the Helium-Neon laser to be superior.

Section Summary: Low Back Pain

The literature on LLLT for low back pain consists of RCTs and several systematic reviews of RCTs. Meta-analyses found that LLLT resulted in significantly greater reductions in pain scores and global assessment scores than a placebo control in the immediate posttreatment setting. Meta-analyses have found conflicting results regarding other outcomes (e.g., disability index, ROM), which were significantly better immediately after treatment with active versus placebo LLLT, though not at longer-term follow-up.

OSTEOARTHRITIC KNEE PAIN

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals who have osteoarthritic knee pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is those who have osteoarthritic knee pain. Also called degenerative arthritis, osteoarthritis (OA) is the most common type of arthritis, which occurs when the cartilage in the knee deteriorates with use and age.

Interventions

The therapy being considered is LLLT.

Comparators

The following practices are currently being used to treat osteoarthritic knee pain: conservative therapy (e.g., physical therapy), medication, and surgery.

Outcomes

General outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Review

Several RCTs and systematic reviews of RCTs have evaluated LLLT for treatment of knee OA, coming to inconsistent conclusions.^{116,117} The most inclusive and up-to-date of these was published by Stausholm et al (2019) and compared LLLT with placebo for knee OA patients.¹¹⁸ To be eligible for inclusion, trials had to report pain, disability, or QOL. A total of 22 trials (N=1063) met the eligibility criteria. Interventions included between 5 to 16 sessions of LLLT or sham LLLT. A total of 9 included studies used a non-recommended dose of LLLT, which had a mean treatment duration of 3.7 weeks. The mean treatment duration was 3.53 weeks in studies using appropriate dosing. The primary outcome was posttreatment pain measured by a 0 to 100 mm VAS score at end of treatment and follow-up (1 to 12 weeks). The mean difference in VAS score was statistically significant favoring LLLT over placebo at end of treatment (14.23 mm; 95% CI, 7.31 to 21.14; $I^2=93\%$) and at follow up (15.92 mm; 95% CI, 6.47 to 25.37; $I^2=93\%$). There was high heterogeneity for the primary outcome, possibly due to differences in the follow-up time period. Risk of bias appeared low. Only 1 study included QOL data, and therefore no QOL meta-analysis was performed.

Tables 12 to 14 summarize the most recent, inclusive meta-analysis for LLLT in knee OA.

Table 12. Trials/Studies Included in Systematic Reviews & Meta-Analysis for Osteoarthritic Knee Pain

Study	Stausholm et al (2019) ¹¹⁸ ,
Al Rashoud et al (2014) ¹¹⁹ ,	●
Alfredo et al (2011, 2018) ^{120, 121} ,	●
Alghadir et al (2014) ¹²² ,	●
Bagheri et al (2011) ¹²³ ,	●
Bülow et al (1994) ¹²⁴ ,	●
Delkhosh et al (2018) ¹²⁵ ,	●
Fukuda et al (2011) ¹²⁶ ,	●
Gur et al (2003) ¹²⁷ ,	●
Gur and Oktayoglu (unpublished)	●
Gworys et al (2012) ¹²⁸ ,	●
Hegedűs et al (2009) ¹²⁹ ,	●
Helianthi et al (2016) ¹³⁰ ,	●
Hinman et al (2014) ¹³¹ ,	●
Jensen et al (1987) ¹³² ,	●
Kheshie et al (2014) ¹³³ ,	●
Koutenaei et al (2017) ¹³⁴ ,	●
Mohammed et al (2018) ¹³⁵ ,	●

Study	Stausholm et al (2019) ^{118,}
Nambi et al (2016) ^{136,}	●
Nivbrant et al (1992) ^{137,}	●
Rayegani et al (2012) ^{138,}	●
Tascioglu et al (2004) ^{139,}	●
Youssef et al (2016) ^{140,}	●

Table 13. Systematic Reviews & Meta-Analysis Characteristics for Osteoarthritic Knee Pain

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Stausholm et al (2019) ^{118,}	1987-2018	22	Patients with OA knee pain	1063 (12-71)	RCT	1-12 weeks

OA: osteoarthritis; RCT: randomized controlled trial.

Table 14. Systematic Reviews & Meta-Analysis Results for Osteoarthritic Knee Pain

Study	VAS (LLLT vs. placebo)	Disability (LLLT vs. placebo)
Stausholm et al (2019) ^{118,}		
At end of therapy		
n	816	617
MD	14.23 mm	0.59
95% CI	7.31 to 21.14	0.23 to 0.86
I^2 (%)	93	57
At follow-up (week 1-12)		
n	581	289
MD	15.92 mm	0.66
95% CI	6.47 to 25.37	0.23 to 1.09
I^2 (%)	93	67

CI: confidence interval; LLLT: low level laser therapy; MD: mean difference; VAS: visual analogue scale.

Section Summary: Osteoarthritic Knee Pain

The literature on LLLT for OA includes RCTs and multiple systematic reviews of RCTs. One of the more recent systematic reviews, which pooled study findings, did find that LLLT significantly reduced pain and improved disability compared with a sham intervention; however, there was high heterogeneity between studies, and individual studies are limited by small sample size and inconsistent timing of follow-up.

HEEL PAIN

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals who have heel pain (ie, Achilles tendinopathy, plantar fasciitis) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals who have heel pain, which can include Achilles tendinopathy, plantar fasciitis, and heel bursitis, etc.

Interventions

The therapy being considered is LLLT.

Comparators

The following practice is currently being used to treat heel pain: conservative therapy (e.g., physical therapy), medication, and surgery.

Outcomes

General outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE**LOWER EXTREMITY TENDINOPATHY OR PLANTAR FASCIITIS****Systematic Review**

Naterstad et al (2022) published a systematic review and meta-analysis of 18 RCTs evaluating LLLT in patients with lower extremity tendinopathy (7 trials of patellar or Achilles tendinopathy) or plantar fasciitis (11 trials).¹⁴¹ In an analysis of LLLT versus any control, both pain and disability were improved with LLLT. VAS scores were reduced immediately after therapy (n=260; SMD, 0.39; 95% CI, 0.09 to 0.7; $I^2=30\%$) and at 4 to 9 weeks follow-up (n=222; SMD, 0.32; 95% CI, 0.05 to 0.59; $I^2=4\%$) compared with control. LLLT did not significantly improve disability compared with other interventions immediately after therapy (n=76; SMD, 0.25; 95% CI, -0.21 to 0.7; $I^2=0\%$) or at 4 to 8 weeks follow-up (n=76; SMD, 0.24; 95% CI, -0.21 to 0.7; $I^2=0\%$).

ACHILLES TENDINOPATHY

Randomized Controlled Trials

Stergioulas et al (2008) randomized 52 recreational athletes with chronic Achilles tendinopathy symptoms to an 8-week (12-session) program of eccentric exercises with LLLT or sham LLLT.²⁵ By intention-to-treat analysis, results for the primary outcome of pain during physical activity assessed on a VAS were significantly lower in the exercise with LLLT group at 4 ($p<.001$), 8 ($p<.001$), and 12 weeks ($p=.007$) after randomization.

Tumilty et al (2012) reported on a randomized, double-blinded, sham-controlled trial of LLLT as an adjunct to 3 months of exercise training in 40 patients with Achilles tendinopathy.¹⁴² Active or sham LLLT was administered 3 times a week for 4 weeks, and exercises performed twice daily for 12 weeks. The primary outcome was the Victorian Institute of Sport Assessment-Achilles Questionnaire at 12 weeks. The only significant difference between groups using intention-to-treat analysis was at 4 weeks for the Victorian Institute of Sport Assessment-Achilles Questionnaire scores, and that difference favored the sham control group. The Victorian Institute of Sport Assessment-Achilles Questionnaire and pain numeric rating scale scores did not differ significantly between the active and the sham groups at 12-week or 1-year follow-ups.

PLANTAR FASCIITIS

Systematic Reviews

Wang et al (2019) published a systematic review and meta-analysis of 6 RCTs comparing LLLT (alone or combined with other interventions) and controls (placebo or other interventions).¹⁴³ A total of 315 adults with plantar heel pain or plantar fasciitis were included in the analysis. Compared with controls, VAS was significantly reduced after treatment (SMD, -0.95; 95% CI, -1.20 to -0.70; $p<.001$), as well as remaining significantly better at 3 months (SMD, -1.13; 95% CI, -1.53 to -0.72; $p<.001$). The meta-analysis was limited by the small number of studies included, small sample size, and insufficient data for longer-term outcomes.

Guimaraes et al (2022) published a systematic review and meta-analysis of 14 studies ($N=817$) comparing LLLT (alone or combined with other interventions) and controls (placebo and other interventions).¹⁴⁴ Compared to the placebo group, LLLT improved pain in the short term of 0 to 6 weeks (4 studies; $n=234$; moderate-quality evidence; MD, -2.28; 95% CI, -2.58 to -1.97; $p<.00001$; $I^2=0\%$). No significant difference in short-term disability was found for individuals in the LLLT group compared to the placebo group. Compared to the conventional rehabilitation alone group, LLLT combined with conventional rehabilitation improved pain in the short term of 0 to 6 weeks (2 studies, $n=90$; moderate-quality evidence; MD, -2.01; 95% CI, -2.89 to -1.13; $p<.00001$; $I^2=0\%$). However, compared to ESWT, LLLT did not significantly reduce pain intensity in the short term (4 studies; $n=175$; low-quality evidence; MD, 0.45; 95% CI, -2.0 to 2.9; $p=.72$; $I^2=94\%$). The meta-analysis was limited by insufficient data for longer-term outcomes, the lack of multicenter studies, and lack of a large sample. Additionally, the quality of evidence for the outcome disability were determined to be low.

Ferlito et al (2023) published a systematic review and meta-analysis on the effects of LLLT on pain intensity and disability in plantar fasciitis.¹⁴⁵ The systematic review included 19 RCTs ($N=1089$). The meta-analysis showed LLLT alone improved plantar fasciitis pain intensity at short-term follow up compared to placebo (3 studies; $n=130$; MD, -22.02; 95% CI, -35.21 to -8.83; $I^2=46\%$; $p=.001$). There was also short-term improved pain intensity in LLLT with exercise compared to exercise alone (4 studies; $n=225$; MD, -21.84; 95% CI, -26.14 to -17.54; $I^2=0\%$;

$p < .00001$). There were several limitations of the systematic review, including the certainty of evidence for most comparisons were very low or low and there was a small number of studies for each comparison. Therefore, further evidence is needed.

Randomized Controlled Trials

A double-blind RCT by Macias et al (2015) assessed 69 patients with unilateral chronic plantar fasciitis and chronic heel pain of 3 months or longer that was unresponsive to conservative treatments (e.g., rest, stretching, physical therapy).¹⁴⁶ Patients were randomized to twice weekly treatment for 3 weeks of LLLT or sham treatment. The primary efficacy outcome (reduction of heel pain pre- to posttreatment) differed significantly between groups ($p < .001$). Mean VAS scores decreased from 69.1 to 39.5 in the LLLT group and from 67.6 to 62.3 in the sham group. The difference in Foot Function Index scores did not differ significantly between groups.

An RCT on LLLT for plantar fasciitis was reported by Kiritsi et al (2010).¹⁴⁷ The trial was double-blind and sham-controlled and assessed 30 patients. Twenty-five (83%) patients completed the trial, with treatment 3 times a week over 6 weeks. At baseline, plantar fascia thickness, measured by ultrasound, was significantly greater in symptomatic feet (5.3 mm) compared with asymptomatic feet (3.0 mm). Plantar fascia thickness decreased in both the LLLT and the sham groups during the trial. Although plantar fascia thickness after 6 weeks of treatment did not differ significantly between groups (3.6 mm in LLLT vs. 4.4 mm in sham), there was a significant between-group difference in the reduction in thickness (1.7 mm LLLT vs. 0.9 mm sham). After night rest or daily activities, VAS scores improved significantly more in the LLLT group (59% improvement) than in the sham group (26% improvement). At baseline, pain after daily activities were rated as 67 out of 100 by both groups. At the end of treatment, VAS scores for daily activities were rated as 28 out of 100 for LLLT and 50 out of 100 for sham.

Cinar et al (2018) conducted a prospective single-blinded RCT investigating combination therapy consisting of LLLT plus exercise and orthotic care versus orthotic care alone in persons with plantar fasciitis.¹⁴⁸ Forty-nine individuals were randomized to LLLT ($n=27$) or a control therapy ($n=22$). Each person performed a home exercise routine and received orthotic care; persons in the LLLT group received treatment 3 times a week for a total of 10 sessions. The function subscale of the American Orthopedic Foot and Ankle Society Score, a VAS, and the 12-minute walk test were used to measure progress. Scores were recorded at baseline, 3 weeks, and 3 months after treatment. At week 3, both groups saw a significant improvement in American Orthopedic Foot and Ankle Society total score (LLLT, $p < .001$; control, $p = .002$). However, at the 3-month follow-up, only the LLLT group progressed as assessed on the American Orthopedic Foot and Ankle Society total score ($p = .04$). At all check-ins, the group scores for the 12-minute walk test were comparable. Both groups showed significant pain reductions at the 3-month follow-up (LLLT, $p < .001$; control, $p = .01$); however, the LLLT group had a more significant reduction in pain at month 3 ($p = .03$). Thus, reviewers concluded that combination therapy plus LLLT was more effective in reducing pain and improving function for patients with plantar fasciitis than orthotic care alone.

Tables 15 and 16 describe the characteristics and results of the RCTs.

Table 15. Summary of Key Randomized Controlled Trial Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Kiritsi et al (2010) ^{147,}	Greece	NR	2006-2007	Patients with unilateral idiopathic PF	LLLT (n=15)	Placebo (n=15)
Macias et al (2015) ^{146,}	US	NR	2011-2013	Patients unilateral chronic PF	LLLT (n=37)	Placebo (n=32)
Cinar et al (2018) ^{148,}	Turkey	NR	2012-2013	Patients with PF	LLLT (n=27)	Control (n=22)

LLLT: low-level laser therapy; NR: not reported; PF: plantar fasciitis.

Table 16. Summary of Key Randomized Controlled Trial Results

Study	Pain	Plantar Fascia Thickness	AOFAS [95%CI]
Kiritsi et al (2010) ^{147,}	VAS (Difference from Baseline)	mm (Difference from Baseline)	NR
LLLT	40 ± 20.3	1.667 ± 0.547	
Placebo	18 ± 8.9	0.920 ± 0.220	
p-value	.001	.007	
Macias et al (2015) ^{146,}	FFI scores (Baseline; Endpoint)	NR	NR
LLLT	111.9 ± 34.2; 82.0 ± 43.6		
Placebo	110.8 ± 32.3; 86.1 ± 43.2		
p-value	.89; .70		
Cinar et al (2018) ^{148,}	VAS (Baseline; 3 months) [95% CI]	NR	
LLLT	6.13; 1.72 [5.41 to 6.85; 0.78 to 2.67]		44.16; 49.95 [42.58 to 45.74; 48.45 to 51.45]
Placebo	5.49; 3.67 [4.67 to 6.31; 2.56 to 4.77]		45.55; 47.78 [43.75 to – 47.34; 46.07 to 49.49]

AOFAS: American Orthopedic Foot and Ankle Society Score; CI: confidence interval; FFI: foot function index; LLLT: low-level laser therapy; NR: not reported; VAS: visual analog scale.

Table 17 displays notable limitations identified in each study.

Table 17. Study Design and Conduct Limitations

Study	Allocation^a	Blinding^b	Selective Reporting^c	Follow-Up^d	Power^e	Statistical^f
Kiritsi et al (2010) ^{147,}	3. Allocation concealment unclear	3. Blinding of outcome assessment unclear				
Macias et al (2015) ^{146,}						
Cinar et al (2018) ^{148,}		3. Blinding of outcome assessment unclear				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

^a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

^b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

^c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

^d Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

^e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

^f Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Heel Pain

Multiple sham-controlled randomized trials have evaluated LLLT for heel pain (Achilles tendinopathy, plantar fasciitis), but findings were inconsistent. A meta-analysis encompassing both lower extremity tendinopathies and plantar fasciitis found significant improvements in pain, but not disability compared with other interventions, and the authors noted the lack of large trials as a concern. One RCT compared LLLT plus therapy with orthotic care alone, and while a significant advantage was observed in LLLT treatment, LLLT treatment was used as a combination therapy. A meta-analysis of Achilles tendinopathy trials found no benefit in pain reduction with LLLT with the exception of at 2 months of follow-up reported in a single trial. A second meta-analysis did find short-term (0 to 6 week) pain improvement in patients receiving LLLT compared to placebo or in combination with conventional rehabilitation, but did not find pain improvement with LLLT compared to ESWT. None of the studies presented long-term follow-up data. Given all factors, further studies are needed to validate the technology.

RHEUMATOID ARTHRITIS

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals who have rheumatoid arthritis (RA) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with RA, a debilitating autoimmune condition that can affect most joints in the body.

Interventions

The therapy being considered is LLLT.

Comparators

The following practices are currently being used to treat RA: conservative therapy (e.g., exercise) and medication, including nonsteroidal anti-inflammatory drugs, steroids, and disease-modifying antirheumatic drugs including biologic agents.

Outcomes

General outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE**Systematic Review**

A Cochrane review by Brosseau et al (2005) included 5 placebo-controlled randomized trials and found that, relative to a separate control group, LLLT reduced pain by 1.10 points on a VAS compared with placebo, reduced morning stiffness duration by 27.5 minutes, and increased tip-to-palm flexibility by 1.3 cm.¹⁴⁹ Other outcomes, such as functional assessment, ROM, and local swelling, did not differ between groups. For RA, relative to a control group using the opposite hand (1 study), no difference was observed between the control and treatment hand for morning stiffness duration, and no significant improvement was reported in pain relief. Reviewers noted that "despite some positive findings, this meta-analysis lacked data on how LLLT effectiveness is affected by 4 important factors: wavelength, treatment duration of LLLT, dosage, and site application over nerves instead of joints."

Lourinho et al (2023) conducted a systematic review and meta-analysis on the effects of LLLT in adults with rheumatoid arthritis.¹⁵⁰ Their literature search was conducted on July 6, 2022 and included 18 RCTs (N=793). There were varying intervention durations of 4 weeks to 6 months among the studies. Also treatment regimens and comparisons varied among the studies. Some studies investigated laser acupuncture, which is out the scope of this review. The meta-analyses for the outcomes of interest, including pain, morning stiffness, handgrip strength, functional

capacity, inflammation, and disease activity, were reported in subgroups of 2 to 4 studies, with no statistically significant differences in effects. The authors noted that 17 of the 18 studies had an overall high risk of bias and the results show a low quality of evidence for LLLT in rheumatoid arthritis.

Randomized Controlled Trial

A randomized, double-blind, placebo-controlled trial assessing outcomes for pain reduction and improvement in hand function in 82 patients with RA treated with LLLT or placebo laser was reported by Meireles et al (2010).¹⁵¹ There were no statistically significant differences between groups for most outcome measurements, including the primary variables, though a few measures significantly favored either the active or placebo treatment. Reviewers concluded that LLLT at the dosage used in the trial was ineffective for treating RA.

Section Summary: Rheumatoid Arthritis

A Cochrane review of 5 placebo-controlled randomized trials found statistically significant improvement of LLLT on some outcomes (e.g., VAS) but not others (e.g., functional assessment). A 2010 RCT, published after the Cochrane review, did not find that LLLT was significantly better than a placebo treatment for most outcomes.

BELL PALSY (FACIAL NERVE PALSY)

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals who have Bell palsy is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with Bell palsy, a condition in which the muscles on 1 side of the face become weak or paralyzed caused by trauma to the seventh cranial nerve.

Interventions

The therapy being considered is LLLT.

Comparators

The following practices are currently being used to treat Bell palsy: conservative therapy (e.g., exercise) and medications, including corticosteroids and antiviral drugs.

Outcomes

General outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months. Outcomes are assessed using the Facial Disability Index and the House-Brackmann Scale.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Randomized Controlled Trials

Alayat et al (2014) reported on a randomized, double-blind, placebo-controlled trial of laser therapy for the treatment of 48 patients with Bell palsy.¹⁵² Facial exercises and massage were given to all patients. Patients were randomized to 1 of 3 groups: high-intensity laser therapy, LLLT, or exercise only. Laser treatment was given 3 times a week to 8 points on the affected side for 6 weeks. At 3 and 6 weeks posttreatment, outcomes were assessed using the Facial Disability Index and the House-Brackmann Scale. Significant improvements in recovery were seen in both laser therapy groups over exercise alone, with the greatest improvement seen with a high-intensity laser.

Ordahan and Karahan (2017) investigated the efficacy of LLLT when used in combination with traditional facial exercises to treat facial paralysis.¹⁵³ Forty-six patients with Bell palsy were randomized to 2 groups: 1 group underwent LLLT plus facial exercise therapy (n=23); the other group underwent facial exercise therapy alone (n=23). Laser therapy was administered 3 times a week for 6 weeks. Patients were evaluated during the treatment and at 3 and 6 weeks posttreatment. The Facial Disability Index was used to evaluate progress. No significant improvement was observed at week 3 in the facial exercise therapy-alone treatment group ($p < .05$), but significant improvement was noted at week 6 ($p < .001$). In the LLLT plus facial exercise therapy group, significant improvement was noted at 3 and 6 weeks ($p < .001$); moreover, improvements in the Facial Disability Index scores in the LLLT plus facial exercise therapy group were significantly greater than those of the facial exercise therapy-alone treatment group at week 3 and week 6 ($p < .05$). Study limitations included lack of long-term follow-up and the use of combination therapy, which obscures the contribution of LLLT.

Nonrandomized Controlled Trials

Wu et al (2023) conducted a nonrandomized trial on the effects of photobiomodulation therapy (PBMT) on Bell palsy (N=54).¹⁵⁴ Patients in the control group (n=27) were recruited prior to patients in the treatment group (n=27). The treatment group received PBMT 3 times per week for 72 sessions. After 6 months, the primary outcomes showed a statistically significant difference between the treatment and control groups in the House-Brackman grading system (RD, -0.59; 95% CI, -0.81 to -0.38; RR, 0.27; 95% CI, 0.13 to 0.56, $p < .001$), Sunnybrook facial grading system (estimated difference, 19.78; 95% CI, 12.31 to 27.24; $p < .001$), and Facial Clinimetric Evaluation Scale (FaCE) (estimated difference, 10.92; 95% CI, 5.58 to 16.27; $p < .001$). The authors conclude limitations of this study include the small sample size and nonrandomized design. Studies with larger sample sizes and randomized designs are needed for further evidence.

Section Summary: Bell Palsy

One RCT found a significant short-term benefit of LLLT over exercise, but long-term outcomes were not available. Another RCT found significant short-term benefit with facial exercise therapy plus LLLT over facial exercise therapy alone, but again, no long-term data were available. One nonrandomized controlled trial found significant differences between the PBMT and control group in primary outcomes; however, the study had a small sample size and nonrandomized design. The limited evidence on laser therapy for Bell palsy is insufficient to draw conclusions. Because Bell palsy often improves within weeks and may resolve completely within months, it is difficult to isolate specific improvements from laser therapy over the natural resolution of the illness. Also, no sham-controlled trials are available.

FIBROMYALGIA**Clinical Context and Therapy Purpose**

The purpose of LLLT in individuals who have fibromyalgia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with fibromyalgia, a disorder characterized by widespread musculoskeletal pain often accompanied by fatigue, sleep, memory, and mood issues. Symptoms can begin after a physical trauma, surgery, or infection or, in some cases, gradually accumulate over time without a single triggering event.

Often, fibromyalgia co-exists with other conditions, including irritable bowel syndrome, migraine, interstitial cystitis, and TMJ disorders.

Interventions

The therapy being considered is LLLT.

Comparators

The following practice is currently being used to treat fibromyalgia: conservative therapy (e.g., exercise) and medications, including pain relievers, antidepressants, and anti-seizure drugs.

Outcomes

General outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months. Outcomes are measured with the Fibromyalgia Impact Questionnaire (FIQ), the McGill Pain Questionnaire, and a pain VAS.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Review

Honda et al (2018) published a systematic review and meta-analysis of RCTs evaluating pain relief modalities for fibromyalgia.¹⁵⁵ Eleven studies with a total of 498 patients (range, 20 to 80) were included; 5 studies evaluated LLLT and the remainder covered other treatment modalities. Compared with control, LLLT was not associated with a reduction of VAS-measured pain (MD, -4.0; 95% CI, -23.4 to 15.4; $p=.69$). LLLT showed a significant reduction in tender points compared with control (MD, -2.21; 95% CI, -3.51 to -0.92; $I^2=42\%$; $p=.0008$) and in the FIQ score (MD, -4.35; 95% CI, -6.69 to -2.01; $I^2=62\%$; $p=.03$). The analysis was limited by its inclusion criteria limited to a pure control group or placebo group for a specific intervention and exclusion of those that used another intervention as a comparator. Several treatment modalities were evaluated and individual pooled results for each intervention had a high degree of heterogeneity.

Randomized Controlled Trials

Several small RCTs evaluating LLLT for fibromyalgia have been published. Navarro-Ledesma et al (2022) randomized 42 patients with fibromyalgia from a single center to active LLLT or placebo for 3 20-minute sessions weekly for 4 weeks.¹⁵⁶ Mean VAS pain scores improved by 3 points on an 11-point numeric scale (95% CI, 2.0 to 3.0; $p<.001$) at the end of intervention with active LLLT compared with placebo.¹⁵⁷ Two weeks after the final treatment the difference between groups was 4 points (95% CI, 3.0 to 5.0; $p<.001$). Health-related QOL, measured on a similar scale, also improved both at the end of treatment (-3; 95% CI, -4.0 to -3.0; $p<.001$) and at follow-up (-4; 95% CI, -5.0 to -4.0; $p<.001$).

Ruaro et al (2014) reported on 20 patients randomized to LLLT or sham treatment 3 times a week for 4 weeks (12 total treatments).¹⁵⁸ Outcomes included scores in the FIQ, which measures physical function, ability to work, pain, fatigue, and depression; the McGill Pain Questionnaire; and a pain VAS. All 3 outcomes were significantly better with active than with sham LLLT posttreatment. Mean overall FIQ scores were 18.6 in the LLLT group and 5.2 in the sham group ($p=.003$). Mean change scores also differed significantly between groups for McGill Pain Questionnaire score ($p=.008$) and VAS score ($p=.002$).

Matsutani et al (2007) randomized 20 patients with fibromyalgia to laser treatment plus stretching exercises or stretching alone.¹⁵⁹ Outcome measures were VAS scores and dolorimetry at tender points, QOL on the FIQ, and the 36-Item Short-Form Health Survey scores. At the end of treatment, both groups demonstrated pain reductions, higher pain thresholds at tender points (all $p<.01$), lower mean FIQ scores, and higher 36-Item Short-Form Health Survey mean scores (all $p<.05$). No significant differences were found between groups.

Section Summary: Fibromyalgia

Few RCTs evaluating LLLT for fibromyalgia are available, some of which have been included in a systematic review and meta-analysis; the existing trials are small. One RCT (N=20 patients) found significantly better outcomes with LLLT than with sham, and another RCT (N=20 patients)

did not find statistically significant between-group differences for similar outcomes. A larger (N=42) study found improved pain and QOL with LLLT; however, the trial was conducted at a single center with strict inclusion criteria. Additional RCTs with sufficient numbers of patients are needed.

CHRONIC NONHEALING WOUNDS

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals with chronic non-healing wounds is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with chronic non-healing wounds: wounds that do not improve after 4 weeks or heal in 8 weeks. These include diabetic foot ulcers, venous-related ulcerations, non-healing surgical wounds, and pressure ulcers. They are often found on the feet, ankles, heels, calves, and on the hips, thighs, and buttocks of those who cannot walk.

Interventions

The therapy being considered is LLLT.

Comparators

The following practice is currently being used to treat chronic nonhealing wounds: standard wound care, including wound debridement, compression therapy, and antibacterial treatment.

Outcomes

The outcome of interest is complete healing or healing to a degree that permits a procedure that results in complete healing. The effects of LLLT to promote healing are expected to occur from weeks to months.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

An evidence assessment by Samson et al (2004), which evaluated vacuum-assisted and low-level laser wound therapies for the treatment of chronic nonhealing wounds and was prepared for the Agency for Healthcare Research and Quality, was based on 11 studies of LLLT.¹⁶⁰ It stated: "The best available trial [of low-level laser wound therapy] did not show a higher probability of

complete healing at 6 weeks with the addition of low-level laser compared with sham laser treatment added to standard care. Study weaknesses were unlikely to have concealed existing effects. Future studies may determine whether different dosing parameters or other laser types may lead to different results."

A Cochrane review by Chen et al (2014) evaluated RCTs on light therapy, including phototherapy, ultraviolet, and laser, for pressure ulcers.¹⁶¹ The few trials available for analysis were of small size and very low quality. Reviewers found the available evidence overall insufficient to conclude whether light therapy is effective on pressure ulcers.

Machado et al (2017) also published a systematic review evaluating the treatment of pressure ulcers with LLLT.¹⁶² Reviewers identified 4 studies meeting eligibility requirements (N=210). Outcomes were the ulcer area, healing rate, and overall healing rate. Two of the 4 studies used LLLT with a single wavelength,^{163,164} and the other 2 used LLLT with probe cluster, which employs the simultaneous assimilation of different types of diodes and wavelengths.^{165,166} In the study that employed the 658 nm wavelength, reviewers found that particular frequency reduced pressure ulcers by 71%. The other wavelengths did not produce any significant findings related to the study outcome; moreover, the studies using the probe cluster technique were also not successful in producing significant findings. While studies should be conducted to investigate further the success found in single wavelength at 658 nm, at this time there is insufficient evidence to suggest LLLT can significantly benefit patients with pressure ulcers.

Li et al (2018) published a systematic review and meta-analysis of 7 RCTs (N=194) evaluating LLLT as a treatment for a diabetic foot ulcer.¹⁶⁷ Ulcer area was significantly reduced with LLLT compared with control (WMD, 34.18; 95% CI, 19.38 to 48.99; $p<.001$), and the complete healing rate significantly improved with LLLT (odds ratio [OR], 6.72; 95% CI, 1.99 to 22.64; $p=.002$). The analysis was limited by the number of studies included and small sample size, and by each study having different parameters, demographic information, ulcer characteristics, follow-up time, and treatment period.

Section Summary: Chronic Nonhealing Wounds

Multiple systematic reviews of the literature did not find sufficient evidence from controlled studies demonstrating that LLLT is effective for wound healing.

LYMPHEDEMA

Clinical Context and Therapy Purpose

The purpose of LLLT in individuals with lymphedema is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with lymphedema or swelling in 1 or both arms and legs. It is commonly caused by the removal of a lymph node. The resulting blockage of the lymphatic system prevents lymph fluid from draining well, leading to fluid build-up and swelling. Other symptoms can include heaviness or tightness in the affected limb, restricted range of motion, aching or discomfort, recurring infections, and dermal fibrosis. Risk factors for developing

lymphedema after cancer from cancer treatment or from other secondary causes can include older age, obesity, and rheumatoid or psoriatic arthritis.

Interventions

The therapy being considered is LLLT.

Comparators

The following practice is currently being used to treat lymphedema: conservative care (e.g., exercise), pneumatic compression, and complete decongestive therapy.

Outcomes

General outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms and treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

Several systematic reviews of RCTs and observational studies have been published. For example, Smoot et al (2015) published a systematic review of studies on the effect of LLLT on symptoms in women with breast cancer-related lymphedema.¹⁶⁸ Reviewers identified 9 studies, 7 RCTs, and 2 single-group studies. Three studies had a sham control group, 1 used a waitlist control, and 3 compared LLLT with an alternative intervention (e.g., intermittent compression). Only 3 studies had blinded outcomes assessments, and in 3 studies, participants were blinded. A pooled analysis of 4 studies found significantly greater reductions in upper-extremity volume with LLLT than with the control condition (pooled effect size, -0.62; 95% CI, -0.97 to -0.28). Only 2 studies were suitable for a pooled analysis of the effect of LLLT on pain. This analysis did not find a significant difference in pain levels between LLLT and control (pooled effect size, -1.21; 95% CI, -4.51 to 2.10).

Omar et al (2012) published a qualitative systematic review of LLLT for the management of breast cancer-related lymphedema.¹⁶⁹ They selected 8 studies (N=230) for their review. Five studies were graded as Sackett evidence level II (small randomized trial with high false-positive or false-negative errors), 2 were graded as level III (nonrandomized comparative study), and 1 study was graded as level V evidence (case series). Reviewers noted major methodologic flaws and little uniformity in trial designs.

Chiu et al (2023) published a systematic review and meta-analysis on LLLT on the treatment of breast cancer-related lymphedema.¹⁷⁰ The systematic review included 11 RCTs published between 2003 and 2021. There were positive effects in the LLLT group compared to the control group in post-treatment QOL (3 studies; n=73; SMD, 0.47; 95% CI, 0.00 to 0.94; $I^2=0\%$; p=.05), reduction in swell at post-treatment (6 studies; n=204; SMD, -0.41; 95% CI, -1.01 to 0.18; $I^2=76\%$; p=.18), and reduction in swelling at 1 to 3 months post-treatment (5 studies; n=193; SMD, -1.06; 95% CI, -2.11 to -0.02; $I^2=90\%$; p=.05). Overall, limitations included a high heterogeneity among studies and varying follow-up periods among studies. The authors note larger studies with long-term follow-up are needed.

Randomized Controlled Trial

One of the larger double-blind RCTs was published by Omar et al (2011); it reported on 50 patients with postmastectomy lymphedema.¹⁶⁹ The average length of time that patients had swelling was 14 months (range, 12 to 36 months). They were treated with active or sham laser 3 times a week for 12 weeks over the axillary and arm areas. Also, all participants were instructed to perform daily arm exercises and to wear a pressure garment. Limb circumference, shoulder mobility, and grip strength were measured before treatment and at 4, 8, and 12 weeks. Limb circumference declined over time in both groups, with significantly greater reductions in the active laser group at 8 (20.0 cm vs. 16.4 cm), 12 (29 cm vs. 21.8 cm), and 16 (31 cm vs. 2 cm) weeks. Shoulder flexion and abduction were significantly better in the active laser group at 8 and 12 weeks. Grip strength was significantly better in the active laser group after 12 weeks (26.2 kg vs. 22.4 kg). The durability of these effects was not assessed.

Section Summary: Lymphedema

Several systematic reviews of RCTs and observational studies found methodologic flaws in the available studies and collectively these studies did not consistently report better outcomes in patients receiving LLLT versus a control condition for treatment of lymphedema.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Orthopaedic Surgeons

In 2016, the American Academy of Orthopaedic Surgeons' guidelines on the management of carpal tunnel syndrome indicated the: "limited evidence supports that laser therapy might be effective compared to placebo."¹⁷¹

American College of Physicians

In 2017, the American College of Physicians (ACP) released guidelines relating to noninvasive treatments for chronic low back pain.¹⁷² The guidelines strongly recommended that patients with chronic low back pain should first seek nonpharmacologic treatment such as exercise,

multidisciplinary rehabilitation, acupuncture, and mindfulness-based stress reduction-all based on moderate quality evidence. The recommendation also stated that patients with chronic low back pain should seek treatments such as tai chi, yoga, motor control exercise, progressive relaxation, electromyography biofeedback, LLLT, operant therapy, cognitive behavioral therapy, or spinal manipulation-all based on low-quality evidence. While the ACP stated that LLLT has a small effect on pain and function, it found the evidence insufficient for the use of LLLT.

In 2020, the ACP published a joint guideline on management of acute pain from non-low back musculoskeletal injuries with the American Academy of Family Physicians.¹⁷³ No recommendations are made specific to LLLT, but the guideline notes that laser therapy did not significantly reduce pain in 1 to 7 days compared to placebo.

American Physical Therapy Association

In 2018, the American Physical Therapy Association published an updated guideline on the diagnosis and treatment of Achilles tendinitis.¹⁷⁴ The use of LLLT was given a level D recommendation, meaning that no recommendation could be made due to contradictory evidence. This is a change from the previous version of the guideline published in 2010, which gave LLLT a level B recommendation.¹⁷⁵

Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology

In 2017, the Mucositis Prevention Guideline Development Group published guidelines on preventing oral and oropharyngeal mucositis in children undergoing hematopoietic cell transplantation.¹⁷⁶ The guidelines were based on an evidence review consisting of randomized controlled trials that evaluated interventions such as cryotherapy and low-level laser therapy (LLLT). The guidelines suggested that LLLT could be offered to children but classified this recommendation as weak.

In 2020, the Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology published joint guidelines on the management of mucositis secondary to cancer therapy.¹⁷⁷

For the prevention of oral mucositis, the 2 associations recommended the following treatments, based on level 1 evidence: LLLT in patients undergoing radiotherapy with chemotherapy for head and neck cancer; LLLT in patients receiving hematopoietic cell transplantation conditioned with high-dose chemotherapy with or without total body irradiation; recombinant human keratinocyte growth factor-1 in patients receiving high-dose chemotherapy and total body irradiation, followed by autologous cell transplantation for hematologic malignancy; and benzydamine mouthwash in patients with head and neck cancer receiving moderate-dose radiotherapy without concomitant chemotherapy.

Additionally, numerous treatments were recommended for the prevention of oral mucositis based on level II evidence, including LLLT in patients undergoing radiotherapy, without concomitant chemotherapy, for head and neck cancer. Several LLLT protocols are outlined by the guideline based on cancer treatment modality, ranging in wavelength from 632.9 to 660 nm.

National Institute for Health and Care Excellence

In 2009, NICE issued guidance on early management of persistent, nonspecific low back pain and did not recommend laser treatment, citing limited evidence.¹⁷⁸ The 2016 and 2020 updated guidance does not mention laser therapy.¹⁷⁸

North American Spine Society

In 2020, the North American Spine Society published a guideline on the diagnosis and treatment of low back pain.¹⁷⁹ The guideline was based on a systematic review of the literature to address key clinical questions regarding the diagnosis and treatment of adults with nonspecific low back pain. Recommendations specific to laser therapy are summarized in Table 18.

Table 18. North American Spine Society Guideline Recommendations for Laser Therapy

Guideline Recommendation	Grade of Recommendation
"It is suggested that the combination of laser therapy (low-level or high-level) with exercise provides better short-term relief of pain than either exercise or laser therapy alone."	B
"There is conflicting evidence that the combination of laser therapy with exercise provides better short-term improvement in function compared to exercise or laser therapy alone."	I
"It is suggested that there is no short-term benefit of laser therapy (low-level or high-level) when compared with exercise alone."	B

Grade of Recommendation (levels of evidence range from Level I [high quality randomized controlled trial] to Level V [expert consensus]): A=Good evidence (Level I studies with consistent findings) for or against recommending intervention; B=Fair evidence (Level II or III studies with consistent findings) for or against recommending intervention; C=Poor quality evidence (Level IV or V studies) for or against recommending intervention; I=Insufficient or conflicting evidence not allowing a recommendation for or against intervention.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 19.

Table 19. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT05763381	Photobiomodulation Therapy for Plantar Fasciitis: A Single-Blind Randomized Control Trial	100	Sep 2025
NCT05763706	Evaluating the Efficacy of Photobiomodulation Therapy in the Management of Chemotherapy-induced Peripheral Neuropathy: a Randomized Controlled Trial	172	Mar 2030

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT04690439	Evaluating the Effectiveness of Photobiomodulation Therapy in the Management of Breast Cancer-related Lymphedema: a Randomized Controlled Trial	104	Feb 2028
NCT05242991	Comparison of Two Photobiomodulation Protocols for the Oral Mucositis and Xerostomia Prevention in Irradiated Head and Neck Cancer Patients: a Randomized, Multicenter, Single-blind Controlled Clinical Trial	132	Oct 2024
NCT04596410	Double-blind, Randomized, Multi-center, Non-inferiority Clinical Trial Comparing Two Photobiomodulation Protocols in the Analgesia of Chemotherapy-induced Oral Mucositis in Children	406	Feb 2024
NCT03945240	Evaluating Different Low-level Laser Therapies to Treat Neck Pain in Air Force Pilots and Flight Crew	296	Sep 2025
<i>Published</i>			
NCT05585333	Photobiomodulation Therapy for Facial Paralysis Over 8 Weeks: An Open-Label Pilot, Non-concurrent Control Study	54	May 2022
NCT04784377	High Intensity Versus Low Level Laser Therapy in Treatment of Patients With Subacromial Impingement Syndrome: A Randomized, Double-blind, Controlled Trial	42	Sep 2022

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
97037	Application of a modality to 1 or more areas; low-level laser therapy (ie, nonthermal and non-ablative) for post-operative pain reduction
0552T	Low-level laser therapy, dynamic photonic and dynamic thermokinetic energies, provided by a physician or other qualified health care professional
S8948	Application of a modality (requiring constant provider attendance) to one or more areas; low-level laser; each 15 minutes

REVISIONS	
2005	Policy added to the bcbsks.com web site.
03-12-2013	Title Revised from "Low-Level Laser Infrared Therapy (also known as soft laser therapy, Microlight 830, and cold laser therapy)" to "Low-Level Laser Therapy"
	Description section updated
	In Policy section: <ul style="list-style-type: none"> Revised policy language from, "Low-level laser treatment is considered experimental/investigational for all indications, including but not limited to carpal tunnel syndrome and other pain disorders, edema, and to enhance wound healing due to the lack of sufficient studies and published scientific literature." to, "Low-level laser therapy is considered experimental/investigational for all indications, including but not limited to carpal tunnel syndrome." This policy language change does not change the intent of the policy position. Added the Policy Guidelines of: "Other protocols have used low-level laser energy applied to acupuncture points on the fingers and hand. This technique may be referred to as "laser acupuncture." Laser acupuncture is not reviewed in this policy."
	Added Rationale section
	In Coding section: <ul style="list-style-type: none"> Added coding notations.
	Added Revision section
	Added References
02-10-2015	Description section updated
	In the Policy section: <ul style="list-style-type: none"> Added to policy statement "treatment of" to read, "Low-level laser therapy is considered experimental / investigational for all indications, including but not limited to treatment of carpal tunnel syndrome." This wording change does not change the intent of the policy.
	Rationale section updated

REVISIONS	
	References updated
07-20-2016	Description section updated.
	In Policy section: <ul style="list-style-type: none"> ▪ In the policy statement moved "treatment of carpal tunnel syndrome" to a list of experimental / investigational indications, adding indications 2 through 13: <ol style="list-style-type: none"> 1. Carpal tunnel syndrome 2. Neck pain 3. Subacromial impingement 4. Adhesive capsulitis 5. Temporomandibular joint pain 6. Low back pain 7. Osteoarthritis knee pain 8. Heel pain (i.e., Achilles tendinopathy, plantar fasciitis) 9. Rheumatoid arthritis 10. Bell palsy 11. Fibromyalgia 12. Wound healing 13. Lymphedema"
	Rationale section updated
	References updated
11-12-2018	Description section updated
	In Policy Section: <ul style="list-style-type: none"> ▪ Added "Low-level laser therapy may be considered medically necessary for prevention of oral mucositis in patients undergoing cancer treatment associated with increased risk of oral mucositis, including chemotherapy and/or radiotherapy, and/or hematopoietic cell transplantation (see Policy Guidelines)." In Policy Guidelines: <ul style="list-style-type: none"> ▪ Added "In the meta-analysis of 18 trials comparing low-level laser therapy (LLLT) to chemotherapy or chemoradiation for prevention of oral mucositis (Oberoi et al [2014]), the course of LLLT was generally from day 0 through treatment. In studies of hematopoietic cell transplant, the course of LLLT began between day -7 and day 0 and continued as long as day 14 or 15. In studies that began LLLT at day -7 or day -5 before hematopoietic cell transplant, the course of laser therapy ended at day -1 or day 0."
	Rationale section updated
	In Coding section: <ul style="list-style-type: none"> ▪ Added the following ICD-10 neoplasm Code Ranges: C00.0-C14.8, C15.3-C26.9, C30.0-C39.9, C40.0-C41.9, C43.0-C44.99, C45.0-C49.A9, C50.011-C50.929, C51.0-C58, C60.0-C63.9, C64.1-C68.9, C69.00-C72.9, C73-C75.9, C7A.010-C7A.8, C7B.00-C7B.8, C76.00-C80.2, C81.00-C96.9, D00.00-D09.9, D37.01-D48.9, D49.0-D49.9 ▪ Removed "Experimental / Investigational for all diagnoses related to this medical policy." Statement.
	References updated
07-01-2019	In Coding section: <ul style="list-style-type: none"> ▪ Added CPT code: 0552T
08-14-2019	Description updated
	Rationale section updated
	References updated
04-19-2021	Description updated
	Rationale section updated
	References updated
08-19-2021	Description updated

REVISIONS	
	Rationale section updated
	References updated
10-01-2021	In Coding section (Effective 10-01-2021) <ul style="list-style-type: none"> Added ICD-10 codes C56.3; C79.63; C84.7A
07-26-2022	Updated Description Section
	Updated Rationale Section
	Updated Coding Section <ul style="list-style-type: none"> Removed coding bullets <ul style="list-style-type: none"> There is no ICD-10-CM diagnosis code for risk of oral mucositis. Codes such as K12.31, T45.1X5, and Y84.2 would require that the mucositis or adverse events had occurred. Medically necessary claims for patients receiving cancer treatment would be coded with a code from the Neoplasms (C00-D49) code range.
	Updated References Section
07-25-2023	Updated Description Section
	Updated Rationale Section
	Updated Coding Section <ul style="list-style-type: none"> Removed ICD-10 Codes
	Updated References Section
01-01-2024	Updated Coding Section <ul style="list-style-type: none"> Added new code 97037 (eff. 01-01-2024)
07-23-2024	Updated Description Section
	Updated Rationale Section
	Updated References Section

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