2.01.56	Low-Level Laser Therapy		
Original Policy Date:	March 1, 2006	**Effective Date:**	September 1, 2019
Section:	2.0 Medicine	**Page:**	Page 1 of 38

Policy Statement

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).

Low-level laser therapy is considered **investigational** for all other indications including but not limited to:

- Adhesive capsulitis
- Bell palsy
- Carpal tunnel syndrome
- Fibromyalgia
- Heel pain (i.e., Achilles tendinopathy, plantar fasciitis)
- Low back pain
- Lymphedema
- Neck pain
- Osteoarthritic knee pain
- Rheumatoid arthritis
- Subacromial impingement
- Temporomandibular joint pain
- Wound healing

Policy Guidelines

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 (HCT), 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.

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 herein.

Coding

There is no specific CPT code for LLLT. However, providers may use the following CPT code because the laser emits light in the infrared spectrum:

- **97026**: Application of a modality to 1 or more areas; infrared

The following HCPCS code is specific to this therapy:

- **S8948**: Application of a modality (requiring constant provider attendance) to one or more areas; low-level laser; each 15 minutes

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.

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.

Related Policies

- Temporomandibular Joint Disorder
- Treatment of Tinnitus

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. 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.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

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

Device	Manufacturer	Date Cleared	510(k) No.	Indication
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. 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 GRTLITE™ 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 LLT devices have received 510(k) clearance from the FDA; most recently, in 2018,

Super Pulsed Laser technology (Multi Radiance Medical) was approved by the FDA through the premarket approval process for use in neck and shoulder pain.

Rationale

Background

Oral Mucositis

Oral mucositis describes inflammation of the oral mucosa and typically manifests as erythema or ulcerations that appear seven to ten 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 narcotic 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 two to four weeks after cessation of cytotoxic chemotherapy. Low -level laser therapy (LLLT) has been used in cancer therapy-induced oral mucositis in patients treated with radiotherapy and/or chemotherapy and hematopoietic cell transplantation.

Musculoskeletal and Neurologic Disorders

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 nine 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, patients experience marked sensory loss and significant functional impairment with thenar atrophy.

Treatment

Mild-to-moderate cases of CTS 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. Patients 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. LLLT is also used to treat CTS.

Low-Level Laser Therapy

LLLT 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.

LLLT is being evaluated to treat a wide variety of conditions, including soft tissue injuries, myofascial pain, tendinopathies, nerve injuries, joint pain, and lymphedema.

Literature Review

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, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one 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. RCTs 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.

Prevention of Oral Mucositis

Clinical Context and Therapy Purpose

The purpose of low-level laser therapy (LLLT) in patients 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 question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have an increased risk of oral mucositis due to some cancer treatments and/or HCT?

The following PICOs were used to select literature to inform this review.

Patients

The relevant population of interest are 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. LLLT is provided in an outpatient setting and may be administered by physical therapists and other practicing alternative medicine.

Comparators

Oral mucositis usually heals two to four 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

The 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:

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

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,] Patients were randomized to 650 nm laser, 780 nm laser, or placebo. Patients in the 650 nm laser group were more likely to have received a total body irradiation-containing regimen than the other 2 groups; otherwise, the groups were comparable. LLLT began on the first day of conditioning and continued for three days posttransplant. Of the 70 patients, 47 (67%) had complete or nearly complete mucositis measurements over time; the average number of visits per patient was similar among the 3 groups. The difference between groups in mean oral mucositis scores was greatest at day 11 (650 nm, 16.7; 780 nm, 20.6; placebo, 24.3), but this difference between the 650 nm group and placebo group was not statistically significant (p=0.06). Patient-specific oral mucositis scores differed significantly between the two groups only when adjusted for total body irradiation exposure. Of the 70 patients in the trial, 17 (24%) were assessed for oral pain. With group sizes of 5 and 6, the 650 nm group had significantly lower patient-specific average pain scores (15.6) than the placebo group (47.2). No adverse events from LLLT were noted. 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 relates to the three 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.[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.[4,] Eight RCTs assessed patients undergoing HCT, eight 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 3-4) decreased with prophylactic LLLT, with a relative risk of 0.37 (95% confidence interval [CI], 0.20 to 0.67; p=0.001). Moreover, the absolute risk reduction in the incidence of severe mucositis (-0.35) significantly favored LLLT (95% CI, -0.48 to -0.21; p<0.001). 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.

Randomized Controlled Trials

Two of the larger RCTs evaluating LLLT for prevention of oral mucositis were published by Gautam et al (2012).[6,NA7,] One reported on LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 121 oral cancer patients.[7,] The other reported on LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 221 head and neck cancer patients.[6,] There is an apparent overlap in patients in these 2 reports, with the head and neck cancer study including the 121 patients with a primary tumor site in the oral cavity. Patients in these studies received LLLT before radiotherapy at 66 gray delivered daily in 33 fractions, 5 days per week, and concurrent with cisplatin. LLLT was delivered at a wavelength of 632.8 nm, power density of 24 mW/cm^2, and a dosage of 3 to 3.5 J. In the report on oral cancer, LLLT before radiotherapy led to significant reductions in the incidence of severe oral mucositis (29% vs 89%) and its associated pain (18% vs 71%, with a VAS score >7), opioid analgesic use (7% vs 21%), and total parenteral nutrition (30% vs 39%), all respectively, during the last weeks of chemoradiotherapy. LLLT also reduced the duration of severe oral mucositis (4.07 days vs 13.96 days), severe pain (5.31 days vs 9.89 days), and total parenteral nutrition (14.05 days vs 17.93 days), all respectively. In the 221 patients treated for head and neck cancer, LLLT led to significant reductions in the incidence and duration of severe oral mucositis (8.19 days vs 12.86 days) and its associated pain (VAS score, 4 vs 7), total parenteral nutrition (45.0% vs 65.5%), and opioid analgesic use (9% vs 26% for step III), all respectively. Gautam et al (2013) assessed patient-reported on outcomes from the same study of 221 head and neck cancer patients using the Oral Mucositis Weekly Questionnaire-Head and Neck and the Functional Assessment of Cancer Treatment-Head and Neck questionnaire.[8,] Patients received LLLT as described above. Patients in the LLLT group reported significantly better outcomes than the placebo group, with lower scores on both the Oral Mucositis Weekly Questionnaire-Head and Neck ($p<0.001$) and Functional Assessment of Cancer Treatment-Head and Neck questionnaire ($p<0.05$).

In 2015 and 2016, 3 relatively small (i.e., each <50 patients), double-blind, sham-controlled, randomized trials on prevention of oral mucositis in patients undergoing cancer treatment were published. Gautam et al (2015) reported on 46 patients with head and neck cancer scheduled for radiotherapy and found significant reductions in the incidence and duration of severe oral mucositis ($p=0.002$) and severe pain ($p=0.023$) after LLLT vs sham.[9] Oton-Leite (2015) reported on 30 head and neck cancer patients undergoing chemoradiation and found that oral mucositis grades were significantly lower in the LLLT group than in the control group at week 1, 3, and 5 evaluations.[10] For example, at the last clinical evaluation (week 5), the rates of grade 3 oral mucositis were 25% in the LLLT group and 54% in the control group. Ferreira et al (2016) evaluated 36 patients with hematologic cancer undergoing HCT.[9,] The overall incidence of oral mucositis did not differ significantly between groups ($p=0.146$). However, the rate of severe oral mucositis (grade 3 or 4) was significantly lower in the laser group (18%) than in the control group (61%; $p=0.015$).

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. Review of the key study evaluated by the MASCC/ISOO investigators for this recommendation revealed limitations that included statistically nonsignificant findings for the primary outcome measure. 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. A 2014 systematic review of LLLT for prevention of oral mucositis 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. Also, 3 double-blind RCTs published in 2015 and 2016 found significantly better outcomes in patients undergoing LLLT compared with sham treatment before or during cancer treatment.

Carpal Tunnel Syndrome
Clinical Context and Therapy Purpose
The purpose of LLLT in patients who have CTS is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have CTS?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have 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, which is frequently diagnosed between the ages of 30-60. 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 ATP production and cellular respiration, and improvement of blood circulation to remove algesic substances.

Comparators
The following therapies are currently being used include 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:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

A TEC Assessment (2010) evaluated LLLT for CTS and chronic neck pain.[10,] For inclusion in the Assessment, studies had to: 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 two 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 seven 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 six of the eight 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 (threestudies) and greater improvement in VAS scores (two 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: CTS
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 (six of eight). 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 patients who have neck pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have neck pain?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have 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 therapies are currently being used include 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 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:

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

The TEC Assessment (2010), which included 6 trials of LLLT for chronic neck pain, found inconsistent results.[10,] In the largest study (Chow et al [2006]), 90 patients were randomized to active LLLT or sham treatment.[14,] Five weeks after the seven-week treatment period, patients in the active treatment group reported a 2.7-point improvement in VAS pain score vs 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.[15,] 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 two 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 patients who have SAIS is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have SAIS?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have SAIS, 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 therapies are currently being used include 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 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.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

Several RCTs evaluating LLLT for treatment of SAIS have been published. Two sham-controlled studies, by Yeldan et al (2009)[16,] and by Dogan et al (2010),[17,] 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).[18,]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 vs conservative treatment. In a study designed to assess the effectiveness of LLLT in patients with SAIS, Bal et al (2009) randomized 44 patients to a 12-week home exercise program with or without LLLT.[19,] Outcome measures of night pain, Shoulder Pain and Disability Index, 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 Shoulder Pain and Disability Index scores at 2- and 12-week assessments, but the differences between groups were not statistically significant.
Calis et al (2011) randomized 52 patients with SAIS to LLLT, ultrasound, or exercise.[20,] Patients were treated five days a week for three weeks with hotpack plus ultrasound plus exercise, hotpack plus LLLT plus exercise, or hotpack plus exercise. All three groups showed improvements from baseline to posttreatment in pain at rest, ROM, and function, but between-group improvements with LLLT were not statistically significant.

Table 2. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Yeldan (2009)[16,]	Turkey	1	NR	Patients with SAIS	LLLT (n=34)	Placebo (n=33)
Bal (2009)[19,]	Turkey	1	NR	Newly-diagnosed SAIS patients	LLLT + 12-wk home exercise program (n=22)	12-wk home exercise program (n=22)

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
Dogan (2010)[17,]	Turkey	NR	NR	Patients with SAIS	LLLT (n=30)	Placebo (n=22)
Abrisham (2011)[18,]	Iran	1	NR	Patients with subacromial syndrome (rotator cuff and biceps tendinitis)	LLLT (n=40)	Placebo (n=40)
Calis (2011)l[20,]	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)

LLLT: low-level laser therapy; RCT: randomized controlled trial; NR: not reported; SAIS: subacromial impingement syndrome.

Table 3. Summary of Key RCT Results

Study	Pain	ROM (°)
Yeldan (2009)[16,]	**VAS-A; VAS-R; VAS-N (Change from Baseline)**	
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	0.94; 0.30; 0.79	
Bal (2009)[19,]	**SPADI (Change from Baseline)**	
LLLT	-37±18.58	
Exercise	-37.2±21.28	
P-value	0.486	
Dogan (2010)[17,]	**VAS (Baseline; Posttreatment)**	
LLLT	7.16±1.64; 3.76±1.45	
Placebo	7.59±1.76; 4.63±2.10	
P-value	0.343; 0.216	
Abrisham (2011)[18,]	**VAS (Post-treatment)**	**Active Flexion, mean**
LLLT	4.4±1.2	43.1±2.5
Placebo	2.9±1.1	25.3±2.4
P-value	0.000	0.000
Calis (2011)[20,]	**VAS at Rest (Pre-; Post-treatment)**	**Flexion (Pre-; 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	0.49; 0.10	0.21; 0.05

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

The purpose of the limitation tables (see Tables 4 and 5) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

Table 4. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Yeldan (2009)[16,]	4. 78.3% of patients included in the analysis were female				1,2. Follow-up duration only 3 weeks
Bal (2009)[19,]	4. 70% of patients included in the analysis were female				

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Dogan (2010)[17],					1,2. Follow-up duration not specified
Abrisham (2011)[18],					1,2. Follow-up duration only 3 weeks
Calis (2011)[20],					

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3.Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 5.Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Yeldan (2009)[16],	2. Allocation not concealed	2. Blinding unclear				
Bal (2009)[19],	3. Allocation concealment unclear	1,2,3. Blinding unclear				
Dogan (2010)[17],	3. Allocation concealment unclear					
Abrisham (2011)[18],	3. Allocation concealment unclear	1,2,3. Blinding not described				
Calis (2011)[20],	3. Allocation concealment unclear	1,2,3. Not blinded				

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive limitations 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: SAIS

The literature on LLLT for SAIS 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 patients who have adhesive capsulitis is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have adhesive capsulitis?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have 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 40-65.

Interventions
The therapy being considered is LLLT.

Comparators
The following therapies are currently being used include 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 treatment-related morbidity. The effects of LLLT to promote healing are expected to occur from weeks to months. Outcomes can be measured using the Shoulder Pain and Disability Index and the Croft Shoulder Disability Questionnaire.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

A Cochrane review by Page et al (2014) evaluated LLLT and other electrotherapy modalities for adhesive capsulitis (i.e., frozen shoulder).[21,] 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 six days. On day six, 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).[22,] 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 four and eight weeks of treatment, and at the end of eight more weeks of follow-up. At the same assessment intervals, significant decreases in Shoulder Pain and Disability Index 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 two 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 patients who have TMJ pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have TMJ?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have TMJ.

Interventions
The therapy being considered is LLLT.

Comparators
The following therapies are currently being used include 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 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:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

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.[23,] Fourteen placebo-controlled randomized trials were identified. Ten 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=0.08). However, meta-analyses did find significantly better functional outcomes (i.e., maximum active mouth opening, maximum passive mouth opening) favoring LLLT. For example, the mean difference (MD) in maximum active mouth opening for active treatment vs 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.[24,] 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 (totaln=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, 0.6; 95% CI, -0.47 to -0.73).

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

Study[2]	Chen (2015)[23,]	Chang (2014)[24,]
Ahrari (2014)	•	•
Demirkol (2014)	•	•
Ferreira (2013)	•	•
Da Silva (2012)	•	•
Sattayut (2012)	•	•
Marini (2010)	•	•
Shirani (2009)	•	•
Emshoff (2008)	•	•
Carrasco (2008)	•	•
Da Cunha (2008)	•	•
Mazzetto (2007)	•	•
Venancio (2005)	•	•
Kulekcioglu (2003)	•	•
Conti (1997)	•	•
Fikackova (2007)		•
Cetiner (2006)		•

Table 7. Systematic Reviews & Meta-Analysis Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Chen (2015)[23,]	2003-2014	14	Patients suffering from TMDs	454 (NR)	RCT	NR
Chang (2014)[24,]	2006-2008	7	Patients suffering from TMDs	NR (NR)	RCT	NR

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

Table 8. Systematic Reviews & Meta-Analysis Results

Study	Pain	MAVO	MPVO
Chen (2015)[23,]	**VAS**		
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	<0.001	0.006	0.06
Chang (2014)[24,]	**VAS**		
ES (95% CI)	-0.60 (-0.47 to -0.73)		

CI: confidence interval; WMD: weighted mean difference; MAVO: maximum active vertical opening; MPVO: maximum passive vertical opening; ES: effect size; VAS: visual analog scale.

In a double-blind, placebo-controlled randomized trial, Shobha et al (2017) investigated the effectiveness of LLLT in patients with TMJ pain.[25,] Forty TMJ patients were evenly randomized to an active or a placebo group. Treatment included two to three weekly sessions of LLLT for a total of eight sessions. Patients were evaluated at baseline, after treatment, and at a 30-day follow-up. Both groups experienced pain reduction at all evaluation points. The most significant pain reduction was reported at the 30-day follow-up (p=0.001). There were no significant differences between groups at baseline (p=0.214), final session (p=0.000), or the 30-day follow-up (p=0.230). For a secondary outcome (the ability to open one's mouth), while both groups showed improvement, the difference between groups was not significant (p=0.330). Therefore, LLLT was determined to have no greater impact on healing or pain reduction over placebo. A study limitation is that magnetic resonance imaging was not used, which is the traditional method for diagnosing TMJs.

Section Summary: TMJ Pain
A number of RCTs and several systematic reviews have evaluated LLLT for TMJ pain. Meta-analyses of these trials had mixed findings. The most recent meta-analysis, which included 14 placebo-controlled randomized trials, did not find a statistically significant impact of LLLT on pain but did find that LLLT significantly improved functional outcomes (e.g., mouth opening). RCTs 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 patients who have low back pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have low back pain?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have 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 therapies are currently being used include 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 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:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

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.[26,] Fifteen RCTs (total 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 (1-12 weeks) follow-up. Longer-term outcomes (i.e., 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 six 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 (5-27 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 (five trials) but not at short-term follow-up (three 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.[27,] Reviewers included trials comparing LLLT with placebo that reported pain and/or functional outcomes and a PEDro quality score. Seven trials (totaln=394 patients; 202 assigned to LLLT, 192 assigned to placebo) were included. Six of the 7 trials were considered high-quality (i.e., 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. ROM and change in pain 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.

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

Study[2]	Glazov (2016)[26,]	Huang (2015)[27,]
Alayat (2014)	•	
Ay (2010)	•	
Basford (1999)	•	•
Djavid (2007)	•	•
Glazov (2009)	•	
Glazov (2014)	•	
Klein (1990)	•	•
Konstantinovic (2011)	•	
Lin (2012)	•	
Okamoto (1989)	•	
Ruth (2010)	•	
Soriano (1998)	•	•
Umegaki (1989)	•	
Vallone (2014)	•	•
Wallace (1996)	•	
Gur (2003)		•
Hsieh (2014)		•

Table 10. Systematic Reviews & Meta-Analysis Characteristics

Study	Dates	Trials	Participants[1]	N (Range)	Design	Duration
Glazov (2016)[26,]	1989-2014	15	Non-pregnant adults with CLBP	1039 (20-144)	RCT	NR
Huang (2015)[27,]	1990-2014	7	Patients with nonspecific CLBP	394 (20-100)	RCT	NR

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

Table 11. Systematic Reviews & Meta-Analysis Results

Study	Pain	Disability Score
Glazov (2016)[26],	VAS (LLLT vs Control)	
WMD	-0.79	
95% CI	-1.22 to -0.36	
I^2	70%	
Huang (2015)[27],	VAS (LLLT vs Control)	(LLLT vs Control)
WMD	-13.57	-12.0
95% CI	-17.42 to -9.72	-2.02 to -21.98
I^2	0%	77.6%

CI: confidence interval; LLLT: low-level laser therapy; WMD: weighted mean difference; VAS: visual analog scale.

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.[29] 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 ($p<0.05$). However, group 2 saw significantly better results in lateral flexion measurements and ODI scores ($p<0.05$). 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 one 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 also found that other outcomes (e.g., disability index, ROM) were significantly better immediately after treatment with active vs placebo LLLT, though not at longer-term follow-up.

Osteoarthritic Knee Pain
Clinical Context and Therapy Purpose
The purpose of LLLT in patients who have OA knee pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have OA knee pain?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have OA knee pain. Also called degenerative arthritis, 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 therapies are currently being used include 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 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:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

Several RCTs and systematic review of RCTs have evaluated LLLT for treatment of knee OA . Huang et al (2015) published a systematic review comparing at least 8 treatment sessions of LLLT with sham laser treatment in knee OApatients.[28,]To be eligible for inclusion, trials had to report pain and/or functional outcomes and a PEDro quality score. Nine trials (totaln=518 patients) met eligibility criteria. In these studies, interventions included between 8 and 20 laser or sham sessions over 2 to 6 weeks. All 9 trials were considered high-quality, as assessed using the PEDro scale (score of ³7; maximum score, 11 points). Primary outcomes were posttreatment pain measured by VAS scores and the Western Ontario and McMaster Universities Arthritis Index scores (pain, function). Meta-analyses did not find that LLLT led to significantly lower pain scores than the sham control, either immediately after treatment or at the three-month follow-up. For example, a meta-analysis of 5 studies that reported 12-week pain scores did not find a statistically significant between-group difference (SMD, -0.06; 95% CI, -0.30 to 0.18). Moreover, there were no statistically significant differences between active and sham laser interventions on Western Ontario and McMaster Universities Arthritis Index stiffness scores or function scores. The secondary outcome (ROM after therapy) also did not significantly favor LLLT over a sham intervention.

Bjordal et al (2017) published a systematic review of placebo-controlled randomized trials to determine the short-term efficacy of physical interventions for pain associated with knee OA .[29,] They selected 36 RCTs. The largest proportion of trials evaluated transcutaneous electrical nerve stimulation (n=11), followed by 8 trials on LLLT and 7 on pulsed electromagnetic fields. Also included were trials on electroacupuncture, manual acupuncture, static magnets, and ultrasound. Reviewers did not report pooled analyses for LLLT for knee OA . In a general qualitative analysis, they found that all the physical interventions except manual acupuncture and ultrasound showed better results with active treatment over placebo.

Section Summary: OA Knee Pain
The literature on LLLT for OA includes RCTs and two systematic reviews of RCTs. The more recent systematic review, which pooled study findings, did not find that LLLT significantly reduced pain and improved function compared with a sham intervention.

Heel Pain
Clinical Context and Therapy Purpose
The purpose of LLLT in patients who have heel pain (i.e., Achilles tendinopathy, plantar fasciitis) is to provide a treatment option that is an alternative to or an improvement on existing therapies. The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have heel pain (i.e., Achilles tendinopathy, plantar fasciitis)?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those 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 therapies are currently being used include 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 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:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

Achilles Tendinopathy
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.[30] 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 ($p<0.001$), 8 ($p<0.001$), and 12 weeks ($p=0.007$) 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.[31] 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 four 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).[32] 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; $p<0.001$), as well as remaining significantly better at 3 months (SMD= -1.13; 95% CI -1.53 to -0.72; $p<0.001$). The meta-analysis was limited by the small number of studies included, its small sample size, and insufficient data for longer-term outcomes.

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).[33,]Patients were randomized to twice weekly treatment for three weeks of LLLT or sham treatment. The primary efficacy outcome (reduction of heel pain pre- to posttreatment) differed significantly between groups (p<0.001). 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).[34,] 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 6weeks. 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 six 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). VAS scores after night rest or daily activities 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 vs orthotic care alone in persons with plantar fasciitis.[35,] 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 three times a week for a total of ten 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, three weeks, and three months after treatment. At week three, both groups saw a significant improvement in American Orthopedic Foot and Ankle Society total score (LLLT, p<0.001; control, p=.002). However, at the three-month follow-up, only the LLLT group progressed as assessed on the American Orthopedic Foot and Ankle Society total score (p=0.04). At all check-ins, the group scores for the 12-minute walk test were comparable. Both groups showed significant pain reductions at the three-month follow-up (LLLT, p<0.001; control, p=0.01); however, the LLLT group had a more significant reduction in pain at month three (p=0.03). 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. Limitations included a lack of a control group, which would have accounted for the natural progression of recovery in patients with plantar fasciitis; another limitation is that the LLLT dose may or may not have been precise enough for the conditions of this study.

Table 12. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Kiritsi (2010)[34,]	Greece	NR	2006-2007	Patients with unilateral idiopathic PF	LLLT (n=15)	Placebo (n=15)
Macias (2015)[33,]	US	NR	2011-2013	Patients unilateral chronic PF	LLLT (n=37)	Placebo (n=32)
Cinar (2018)[35,]	Turkey	NR	2012-2013	Patients with PF	LLLT (n=27)	Control (n=22)

LLLT: low-level laser therapy; NR: not reported; RCT: randomized controlled trial; PF: plantar fasciitis.

Table 13 Summary of Key RCT Results

Study	Pain	Plantar Fascia Thickness	AOFAS-F [95%CI]
Kiritsi (2010)[34],	VAS (Difference from Baseline)	(Difference from Baseline)	
LLLT	40±20.3	1.667±0.547	
Placebo	18±8.9	0.920±0.220	
P-value	0.001	0.007	
Macias (2015)[33],	FFI scores (Baseline; Endpoint)		
LLLT	111.9±34.2; 82.0±43.6		
Placebo	110.8±32.3; 86.1±43.2		
P-value	0.89; 0.70		
Cinar (2018)[35],	VAS (Baseline; 3 months) [95% CI]		
LLLT	6.13; 1.72 [5.41–6.85; 0.78–2.67]		44.16; 49.95 [42.58–45.74; 48.45–51.45]
Placebo	5.49; 3.67 [4.67–6.31; 2.56–4.77]		45.55; 47.78 [43.75–47.34; 46.07–49.49]

CI: confidence interval; RCT: randomized controlled trial; FFI: foot function index; AOFAS: American Orthopedic Foot and Ankle Society Score; LLLT: low-level laser therapy; VAS: visual analog scale.

The purpose of the limitations tables (see Table 14) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

Table 14.Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Kiritsi (2010)[34],	3. Allocation concealment unclear	3. Blinding of outcome assessment unclear				
Macias (2015)[33],						
Cinar (2018)[35],		3. Blinding of outcome assessment unclear				

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive limitations 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

At least two sham-controlled randomized trials have evaluated LLLT for heel pain (Achilles tendinopathy, plantar fasciitis) but findings were inconsistent. 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. 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 patients who have RA is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have RA ?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have RA , a debilitating autoimmune condition that can affect most joints in the body.

Interventions
The therapy being considered is LLLT.

Comparators
The following therapies are currently being used include conservative therapy (e.g., exercise) and medication, including nonsteroidal anti-inflammatory drugs, steroids, disease-modifying antirheumatic drugs, and biologic agents.

Outcomes
The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms 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:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

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.[36,] 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 (one 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 four important factors: wavelength, treatment duration of LLLT, dosage, and site application over nerves instead of joints."

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).[38] 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 rheumatoid arthritis.

Section Summary: RA
A Cochrane review of five placebo-controlled randomized trials found a significant benefit 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
Clinical Context and Therapy Purpose
The purpose of LLLT in patients who have Bell Palsy is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have Bell Palsy?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have Bell Palsy, a condition in which the muscles on one 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 therapies are currently being used include conservative therapy (e.g., exercise, physical therapy) and medications, including corticosteroids and antiviral drugs.

Outcomes
The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms 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:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

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.[37,] Facial exercises and massage were given to all patients. Patients were randomized to one of three groups: high-intensity laser therapy, LLLT, or exercise only. Laser treatment was given three times a week to eight points on the affected side for six weeks. At three and six 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.[40] Forty-six patients with Bell palsy were randomized to 2 groups: 1 group underwent LLLT plus facial exercise therapy (FET; n=23); the other group underwent FET alone (n=23). Laser therapy was administered three times a week for six weeks. Patients were evaluated during the treatment and at three and six weeks posttreatment. The Facial Disability Index was used to evaluate progress. No significant improvement was observed at week three in the FET-alone treatment group ($p<0.05$), but significant improvement was noted at week six ($p<0.001$). In the LLLT plus FET group, significant improvement was noted at three and six weeks ($p<0.001$); moreover, improvements in the Facial Disability Index scores in the LLLT plus FET group were significantly greater than those of the FET-alone treatment group at week three and week six ($p<0.05$). Study limitation included lack of long-term follow-up and the use of combination therapy, which obscures the contribution of LLLT.

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 FET plus LLLT over FET alone, but again, no long-term data were available. 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 patients who have fibromyalgia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have fibromyalgia?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those 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 accumulating over time without a single triggering event.

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

Interventions
The therapy being considered is LLLT.

Comparators
The following therapies are currently being used include conservative therapy (e.g., exercise) and medications, including pain relievers, antidepressants, and anti-seizure drugs.

Outcomes
The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms 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, the McGill Pain Questionnaire, and a pain VAS.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

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

Several small RCTs evaluating LLLT for fibromyalgia have been published. Ruaro et al (2014) reported on 20 patients randomized to LLLT or sham treatment 3 times a week for 4 weeks (12 total treatments).[38] Outcomes included scores in the Fibromyalgia Impact Questionnaire (FIQ), which measures physical function, ability to work, pain, fatigue, and depression; the McGill Pain Questionnaire; and a pain VAS. All three 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=0.003). Mean change scores also differed significantly between groups for McGill Pain Questionnaire score (p=0.008) and VAS score (p=0.002).

Matsutani et al (2007) randomized 20 patients with fibromyalgia to laser treatment plus stretching exercises or stretching alone.[39] 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<0.01), lower mean FIQ scores, and higher 36-Item Short-Form Health Survey mean scores (all p<0.05). No significant differences were found between groups.

Honda et al (2018) published a systematic review and meta-analysis of RCTs evaluating pain relief modalities for fibromyalgia. Eleven studies with a total of 498 patients (range, 20-80) were included.[40] 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=0.69). 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=0.0008) and in Fibromyalgia Impact Questionnaire score (MD -4.35; 95% CI -6.69 to -2.01; I^2= 62%; p=0.03). The analysis was limited by only English language studies and only studies with a pure control group or placebo group (i.e., no other intervention) being included and by the high heterogeneity score for included studies.

Section Summary: Fibromyalgia
Few RCTs evaluating LLLT for fibromyalgia are available; the existing trials are small (i.e., <25 patients each). 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. Additional RCTs with sufficient numbers of patients are needed.

Chronic Nonhealing Wounds
Clinical Context and Therapy Purpose
The purpose of LLLT in patients who have chronic non-healing wounds is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have chronic non-healing wounds?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have chronic non-healing wounds: wounds that do not improve after four weeks or heal in eight 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 can not walk.

Interventions
The therapy being considered is LLLT.

Comparators
The following therapies are currently being used include standard wound care, including wound debridement, compression therapy, and antibacterial treatment.

Outcomes
The general outcomes of interest are change in disease status 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:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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.

An evidence assessment by Samson et al (2004), which evaluated vacuum-assisted and low-level laser wound therapies for treatment of chronic nonhealing wounds and was prepared for the Agency for Healthcare Research and Quality, was based on 11 studies of LLLT.[43] 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.[41,] 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.[42,] Reviewers identified 4studies meeting eligibility requirements (totaln=210 patients). Outcomes were the ulcer area, healing rate, and overall healing rate. Two of the four studies used LLLT with a single wavelength[43,]NA[44,]; and the other two used LLLT with probe cluster, which employs the simultaneous assimilation of different types of diodes and wavelengths.[45,]NA[46,] 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 (total patients, n=194) evaluating LLLT as a treatment for a diabetic foot ulcer.[47,] Ulcer area was significantly reduced with LLLT compared with control (WMD 34.18; 95% CI 19.38–48.99; p<0.001), and the complete healing rate significantly improved with LLLT (OR 6.72; 95% CI 1.99–22.64; p=0.002). 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
Three 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 patients who have lymphedema is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of LLLT improve the net health outcome in those who have lymphedema?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are those who have lymphedema or swelling in one 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 therapies are currently being used include conservative care (e.g., exercise), Pneumatic compression, and complete decongestive therapy.

Outcomes
The general outcomes of interest are improvements in functional outcomes and QOL and a reduction in symptoms 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:
a. a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. c. 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. 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.[48,] Reviewers identified nine studies, seven RCTs and two single-group studies. Three studies had a sham control group, one used a waitlist control, and three compared LLLT with an alternative intervention (e.g., intermittent compression). Only three studies had blinded outcomes assessments and, in three 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 two 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.[49] They selected 8 studies (totaln=230 patients) for their review. Five studies were graded as Sackett evidence level II (small randomized trial with high false-positive or false-negative errors), two were graded as level III (nonrandomized comparative study), and one study was graded as level V evidence (case series). Reviewers noted major methodologic flaws and little uniformity in trial designs.

One of the larger double-blind RCTs was published by Omar et al (2011); it reported on 50 patients with postmastectomy lymphedema.[50] The average length of time that patients had swelling was 14 months (range, 12-36 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
Two 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 vs a control condition for treatment of lymphedema.

Summary of Evidence
Oral Mucositis
For individuals who have increased risk of oral mucositis due to some cancer treatments (e.g., chemotherapy, radiotherapy) and/or HCT who receive LLLT, the evidence includes RCTs and systematic reviews. The relevant outcomes are symptoms, morbid events, QOL, and treatment-related morbidity. A 2014 systematic review included 18 RCTs and found better outcomes with LLLT used to prevent oral mucositis than with control treatments. RCTs published after the systematic review had similar findings. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Musculoskeletal and Neurologic Disorders
For individuals who have CTS who receive LLLT, the evidence includes RCTs and systematic reviews. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. Both a 2016 systematic review and a TEC Assessment (2010) did not find sufficient evidence from RCTs that LLLT improves outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have neck pain who receive LLLT, the evidence includes RCTs and systematic reviews. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. A 2013 systematic review identified 17 trials, most of which were considered low-quality. Only two trials were considered moderate quality, and they found that LLLT led to better outcomes than placebo for chronic neck pain. A TEC Assessment (2010) found conflicting evidence. Additionally, laser types, application dosages, and treatment schedules vary in the available evidence and require further study. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have SAIS who receive LLLT, the evidence includes RCTs. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. Most trials did not show a significant benefit of LLLT compared with sham treatment or with an alternative intervention (e.g., exercise). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have adhesive capsulitis who receive LLLT, the evidence includes RCTs and a systematic review. The relevant outcomes are symptoms, functional outcomes, QOL quality of life, and treatment-related morbidity. A Cochrane review evaluating treatments for adhesive capsulitis identified two RCTs assessing LLLT. Due to the small number of trials and study limitations, reviewers concluded that the evidence was insufficient to permit conclusions about the effectiveness of LLLT for adhesive capsulitis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have TMJ who receive LLLT, the evidence includes RCTs and several systematic reviews. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. Meta-analyses of RCTs had mixed findings. A 2015 meta-analysis, which included 14 placebo-controlled randomized trials, did not find a statistically significant impact of LLLT on pain but did find that LLLT significantly improved functional outcomes (e.g., mouth opening). RCTs have not compared the impact of LLLT with physical therapy. The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals who have low back pain who receive LLLT, the evidence includes RCTs and systematic reviews. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. Meta-analyses of RCTs found that LLLT resulted in a significantly greater reduction in pain scores and global assessment scores than a placebo control in the immediate posttreatment setting. Meta-analyses also found that other outcomes (e.g., disability index, range of motion) were significantly better immediately after treatment with active rather than placebo LLLT but not at longer-term follow-up. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have OA knee pain who receive LLLT, the evidence includes RCTs and systematic reviews. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. A 2015 systematic review, which pooled study findings, did not find that LLLT significantly reduced pain or improved functional outcomes compared with a sham intervention. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have heel pain (i.e., Achilles tendinopathy, plantar fasciitis) who receive LLLT, the evidence includes RCTs. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. Findings of two sham-controlled randomized trials were inconsistent, and while an RCT compared LLLT with standard care lacked long-term follow-up. The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals who have RA who receive LLLT, the evidence includes RCTs and a systematic review. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. A systematic review of RCTs found an inconsistent benefit of LLLT for a range of outcomes. A 2010 RCT, published after the systematic review, did not find that LLLT was significantly better than a placebo treatment on most outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have Bell palsy who receive LLLT, the evidence includes two RCTs. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. The RCT found a significant short-term benefit of LLLT over exercise. Longer-term outcomes (>6 weeks) were not available. Because Bell palsy often improves within weeks and may completely resolve 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. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have fibromyalgia who receive LLLT, the evidence includes RCTs. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. The RCTs evaluating LLLT for treatment of fibromyalgia are small (i.e., <25 patients each). One RCT (n=20 patients) found significantly better outcomes with LLLT than with sham, while another (n=20 patients) did not find statistically significant between-group differences for similar outcomes. Additional RCTs with sufficient numbers of patients are needed to establish the efficacy of LLLT for fibromyalgia. The evidence is insufficient to determine the effects of the technology on health outcomes.

Wound Care and Lymphedema
For individuals who have chronic nonhealing wounds who receive LLLT, the evidence includes RCTs and systematic reviews. The relevant outcomes are symptoms, functional outcomes, QOL , and treatment-related morbidity. The few existing RCTs tend to have small sample sizes and potential risk of bias. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have lymphedema who receive LLLT, the evidence includes RCTs and systematic reviews. The relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. Two systematic reviews detected methodologic flaws in the available studies and did not consistently find better outcomes for patients receiving LLLT than those receiving a control condition for the treatment of lymphedema. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information
Practice Guidelines and Position Statements

Mucositis Prevention Guideline Development Group
The Mucositis Prevention Guideline Development Group (2017) published guidelines on preventing oral and oropharyngeal mucositis in children undergoing hematopoietic cell transplantation.[51,] 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.

Multinational Association of Supportive Care in Cancer et al
The Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology (2014) published joint guidelines on the management of mucositis secondary to cancer therapy.[1,]

For the prevention of oral mucositis, the 2 associations recommended the following treatments, based on strong evidence: LLLT (650 nm, power of 40 mW) in patients receiving hematopoietic cell transplantation conditioned with high-dose chemotherapy with or without total body irradiation; oral cryotherapy in patients receiving bolus 5-fluorouracil chemotherapy; 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, the following treatments were recommended for the prevention of oral mucositis based on weaker evidence: LLLT (»632.8 nm) in patients undergoing radiotherapy, without concomitant chemotherapy, for head and neck cancer; oral care protocols for patients undergoing any cancer treatment; oral cryotherapy in patients receiving high-dose melphalan as conditioning for hematopoietic cell transplantation; and oral zinc supplements in oral cancer patients receiving radiotherapy or chemoradiation.

American Physical Therapy Association

The American Physical Therapy Association (2010) published guidelines on the diagnosis and treatment of Achilles tendinitis.[52] LLLT received a level B recommendation (based on moderate evidence) for decreasing pain and stiffness in patients with Achilles tendinopathy. The guidelines concluded that "given the limited number of studies employing LLLT in this population, additional study is warranted. "The Association (2014) stated in a press release, based on a Cochrane review,[22] that "It could be that low-level laser therapy (LLLT) is a useful electrotherapy modality for treatment of adhesive capsulitis, but the effects are marginal, and evidence is a long way from conclusive...."[53]

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (2009) issued guidance on early management of persistent, nonspecific low back pain and did not recommend laser treatment, citing limited evidence.[54] The 2016 updated guidance does not mention laser therapy.[55]The Institute (2018) released guidance stating that it was considering LLLT and that it would issue and interventional procedures consultation document regarding the safety and efficacy of the treatment; at the time of this writing, the Institute was still in progress of releasing their disclosure.

American College of Physicians and American Pain Society

The joint guidelines by the American College of Physicians and American Pain Society (2007) stated that there is insufficient evidence to recommend LLLT for treatment of low back pain.[56] The 2009 updated guidelines did not mention LLLT.[57] released guidelines relating to noninvasive treatments for chronic low back pain.[58] The guidelines strongly recommended that patients with chronic low back pain should first seek nonpharmacologic treatment such as exercise, multidisciplinary rehabilitation, acupuncture, 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 College stated that LLLT has a small effect on pain and function, it found the evidence insufficient for the use of LLLT.

American Academy of Orthopaedic Surgeons

The American Academy of Orthopaedic Surgeons' (2016) guidelines on the management of carpal tunnel syndrome indicated the: "limited evidence supports that laser therapy might be effective compared to placebo."[59]

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 15.

Table 15. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02696408	Efficacy of Prophylactic Low Level Laser Therapy (LLLT) Performed by Nurses for Decreasing Severity of Oral Mucositis During Hematopoietic Stem Cell (HSC) Transplantation : a Randomized Double-Blind Multicenter Prospective Phase III Trial	194	Jul 2019

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT02296697	Comparison Between the Effects of Low-level Laser Therapy, High Frequency and Wound Dressing on Pressure Ulcers Treatment: a Clinical Randomized Trial	75	Dec 2018 (unknown)
NCT01772706	A Randomized, Double-Blind, Controlled, Multi-center, Phase III Study to Assess Efficacy of Low Level Diode Laser (100 MW, 658 Nm), in the Prevention and Treatment of Radiochemotherapy-induced Mucositis in Head and Neck Cancer	100	Mar 2021
NCT02682992	A Phase II Prospective Trial of Low-Level Laser Therapy for Prevention of Oral Mucositis in Patients Receiving Chemotherapy and Radiation for Head and Neck Cancer	50	Mar 2021
Unpublished			
NCT03080207	Comparison of Efficacy of Platelets / Platelet Enriched Plasma Regard (PRP) Method, Complex Decongestive Physiotherapy and Low LevelLaser in Treatment of Lower Extremity Lymphoedema	45	Jan 2018 (completed)

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

References

1. Lalla RV, Bowen J, Barasch A, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer.* May 15 2014;120(10):1453-1461. PMID 24615748
2. Schubert MM, Eduardo FP, Guthrie KA, et al. A phase III randomized double-blind placebo-controlled clinical trial to determine the efficacy of low level laser therapy for the prevention of oral mucositis in patients undergoing hematopoietic cell transplantation. *Support Care Cancer.* Oct 2007;15(10):1145-1154. PMID 17393191
3. Figueiredo AL, Lins L, Cattony AC, et al. Laser therapy in the control of oral mucositis: a meta-analysis. *Rev Assoc Med Bras (1992).* Sep-Oct 2013;59(5):467-474. PMID 24119379
4. Oberoi S, Zamperlini-Netto G, Beyene J, et al. Effect of prophylactic low level laser therapy on oral mucositis: a systematic review and meta-analysis. *PLoS One.* Sep 2014;9(9):e107418. PMID 25198431
5. Doeuk C, Hersant B, Bosc R, et al. Current indications for low level laser treatment in maxillofacial surgery: a review. *Br J Oral Maxillofac Surg.* Apr 2015;53(4):309-315. PMID 25740083
6. Gautam AP, Fernandes DJ, Vidyasagar MS, et al. Low level laser therapy for concurrent chemoradiotherapy induced oral mucositis in head and neck cancer patients - A triple blinded randomized controlled trial. *Radiother Oncol.* Sep 2012;104(3):349-354. PMID 22884841
7. Gautam AP, Fernandes DJ, Vidyasagar MS, et al. Low Level Helium Neon Laser therapy for chemoradiotherapy induced oral mucositis in oral cancer patients - A randomized controlled trial. *Oral Oncol.* Sep 2012;48(9):893-897. PMID 22502814
8. Gautam AP, Fernandes DJ, Vidyasagar MS, et al. Effect of low-level laser therapy on patient reported measures of oral mucositis and quality of life in head and neck cancer patients receiving chemoradiotherapy--a randomized controlled trial. *Support Care Cancer.* May 2013;21(5):1421-1428. PMID 23224689
9. Gautam AP, Fernandes DJ, Vidyasagar MS, et al. Low level laser therapy against radiation induced oral mucositis in elderly head and neck cancer patients-a randomized placebo controlled trial. *J Photochem Photobiol B.* Mar 2015;144:51-56. PMID 25704314
10. Oton-Leite AF, Silva GB, Morais MO, et al. Effect of low-level laser therapy on chemoradiotherapy-induced oral mucositis and salivary inflammatory mediators in head and neck cancer patients. *Lasers Surg Med.* Apr 2015;47(4):296-305. PMID 25824475
11. Ferreira B, da Motta Silveira FM, de Orange FA. Low-level laser therapy prevents severe oral mucositis in patients submitted to hematopoietic stem cell transplantation: a randomized clinical trial. *Support Care Cancer.* Mar 2016;24(3):1035-1042. PMID 26248655

12. Blue Cross and Blue Shield Technology Evaluation Center (TEC). Low-level laser therapy for carpal tunnel syndrome and chronic neck pain. *TEC Assessment.* Nov 2010;Volume 25:Tab 4. PMID 21638940
13. Li ZJ, Wang Y, Zhang HF, et al. Effectiveness of low-level laser on carpal tunnel syndrome: A meta-analysis of previously reported randomized trials. *Medicine (Baltimore).* Aug 2016;95(31):e4424. PMID 27495063
14. Fusakul Y, Aranyavalai T, Saensri P, et al. Low-level laser therapy with a wrist splint to treat carpal tunnel syndrome: a double-blinded randomized controlled trial. *Lasers Med Sci.* May 2014;29(3):1279-1287. PMID 24477392
15. Chow RT, Heller GZ, Barnsley L. The effect of 300 mW, 830 nm laser on chronic neck pain: a double-blind, randomized, placebo-controlled study. *Pain.* Sep 2006;124(1-2):201-210. PMID 16806710
16. Gross AR, Dziengo S, Boers O, et al. Low level laser therapy (LLLT) for neck pain: a systematic review and meta-regression. *Open Orthop J.* Oct 2013;7:396-419. PMID 24155802
17. Yeldan I, Cetin E, Ozdincler AR. The effectiveness of low-level laser therapy on shoulder function in subacromial impingement syndrome. *Disabil Rehabil.* Nov 2009;31(11):935-940. PMID 19031167
18. Dogan SK, Ay S, Evcik D. The effectiveness of low laser therapy in subacromial impingement syndrome: a randomized placebo controlled double-blind prospective study. *Clinics (Sao Paulo).* Dec 2010;65(10):1019-1022. PMID 21120304
19. Abrisham SM, Kermani-Alghoraishi M, Ghahramani R, et al. Additive effects of low-level laser therapy with exercise on subacromial syndrome: a randomised, double-blind, controlled trial. *Clin Rheumatol.* May 4 2011;30(10):1341-1346. PMID 21538218
20. Bal A, Eksioglu E, Gurcay E, et al. Low-level laser therapy in subacromial impingement syndrome. *Photomed Laser Surg.* Feb 2009;27(1):31-36. PMID 19250050
21. Calis HT, Berberoglu N, Calis M. Are ultrasound, laser and exercise superior to each other in the treatment of subacromial impingement syndrome? A randomized clinical trial. *Eur J Phys Rehabil Med.* Mar 2 2011;47(3):375-380. PMID 21364511
22. Page MJ, Green S, Kramer S, et al. Electrotherapy modalities for adhesive capsulitis (frozen shoulder). *Cochrane Database Syst Rev.* Oct 1 2014;10:CD011324. PMID 25271097
23. Stergioulas A. Low-power laser treatment in patients with frozen shoulder: preliminary results. *Photomed Laser Surg.* Apr 2008;26(2):99-105. PMID 18341417
24. Chen J, Huang Z, Ge M, et al. Efficacy of low-level laser therapy in the treatment of TMDs: a meta-analysis of 14 randomised controlled trials. *J Oral Rehabil.* Apr 2015;42(4):291-299. PMID 25491183
25. Chang WD, Lee CL, Lin HY, et al. A meta-analysis of clinical effects of low-level laser therapy on temporomandibular joint pain. *J Phys Ther Sci.* Aug 2014;26(8):1297-1300. PMID 25202201
26. Shobha R, Narayanan VS, Jagadish Pai BS, et al. Low-level laser therapy: A novel therapeutic approach to temporomandibular disorder - A randomized, double-blinded, placebo-controlled trial. *Indian J Dent Res.* Jul-Aug 2017;28(4):380-387. PMID 28836528
27. Glazov G, Yelland M, Emery J. Low-level laser therapy for chronic non-specific low back pain: a meta-analysis of randomised controlled trials. *Acupunct Med.* Oct 2016;34(5):328-341. PMID 27207675
28. Huang Z, Ma J, Chen J, et al. The effectiveness of low-level laser therapy for nonspecific chronic low back pain: a systematic review and meta-analysis. *Arthritis Res Ther.* Dec 15 2015;17:360. PMID 26667480
29. Koldas Dogan S, Ay S, Evcik D. The effects of two different low level laser therapies in the treatment of patients with chronic low back pain: A double-blinded randomized clinical trial. *J Back Musculoskelet Rehabil.* Jul 2017;30(2):235-240. PMID 27472858
30. Huang Z, Chen J, Ma J, et al. Effectiveness of low-level laser therapy in patients with knee osteoarthritis: a systematic review and meta-analysis. *Osteoarthritis Cartilage.* Sep 2015;23(9):1437-1444. PMID 25914044
31. Bjordal JM, Johnson MI, Lopes-Martins RA, et al. Short-term efficacy of physical interventions in osteoarthritic knee pain. A systematic review and meta-analysis of

randomised placebo-controlled trials. *BMC Musculoskelet Disord.* Jun 22 2007;8:51. PMID 17587446
32. Stergioulas A, Stergioula M, Aarskog R, et al. Effects of low-level laser therapy and eccentric exercises in the treatment of recreational athletes with chronic achilles tendinopathy. *Am J Sports Med.* May 2008;36(5):881-887. PMID 18272794
33. Tumilty S, McDonough S, Hurley DA, et al. Clinical effectiveness of low-level laser therapy as an adjunct to eccentric exercise for the treatment of Achilles' tendinopathy: a randomized controlled trial. *Arch Phys Med Rehabil.* May 2012;93(5):733-739. PMID 22541305
34. Macias DM, Coughlin MJ, Zang K, et al. Low-level laser therapy at 635 nm for treatment of chronic plantar fasciitis: a placebo-controlled, randomized studys. *J Foot Ankle Surg.* Sep-Oct 2015;54(5):768-772. PMID 25769363
35. Kiritsi O, Tsitas K, Malliaropoulos N, et al. Ultrasonographic evaluation of plantar fasciitis after low-level laser therapy: results of a double-blind, randomized, placebo-controlled trial. *Lasers Med Sci.* Mar 2010;25(2):275-281. PMID 19841862
36. Cinar E, Saxena S, Uygur F. Low-level laser therapy in the management of plantar fasciitis: a randomized controlled trial. *Lasers Med Sci.* Jul 2018;33(5):949-958. PMID 29273892
37. Brosseau L, Robinson V, Wells G, et al. Low level laser therapy (Classes I, II and III) for treating rheumatoid arthritis. *Cochrane Database Syst Rev.* Oct 19 2005(4):CD002049. PMID 16235295
38. Meireles SM, Jones A, Jennings F, et al. Assessment of the effectiveness of low-level laser therapy on the hands of patients with rheumatoid arthritis: a randomized double-blind controlled trial. *Clin Rheumatol.* May 2010;29(5):501-509. PMID 20082104
39. Alayat MS, Elsodany AM, El Fiky AA. Efficacy of high and low level laser therapy in the treatment of Bell's palsy: a randomized double blind placebo-controlled trial. *Lasers Med Sci.* Jan 2014;29(1):335-342. PMID 23709010
40. Ordahan B, Karahan AY. Role of low-level laser therapy added to facial expression exercises in patients with idiopathic facial (Bell's) palsy. *Lasers Med Sci.* May 2017;32(4):931-936. PMID 28337563
41. Ruaro JA, Frez AR, Ruaro MB, et al. Low-level laser therapy to treat fibromyalgia. *Lasers Med Sci.* Nov 2014;29(6):1815-1819. PMID 24801056
42. Matsutani LA, Marques AP, Ferreira EA, et al. Effectiveness of muscle stretching exercises with and without laser therapy at tender points for patients with fibromyalgia. *Clin Exp Rheumatol.* May-Jun 2007;25(3):410-415. PMID 17631737
43. Samson D, Lefevre F, Aronson N. Wound-healing technologies: low-level laser and vacuum-assisted closure. *Evid Rep Technol Assess (Summ).* Dec 2004(111):1-6. PMID 15663354
44. Chen C, Hou WH, Chan ES, et al. Phototherapy for treating pressure ulcers. *Cochrane Database Syst Rev.* 2014;7:CD009224. PMID 25019295
45. Machado RS, Viana S, Sbruzzi G. Low-level laser therapy in the treatment of pressure ulcers: systematic review. *Lasers Med Sci.* May 2017;32(4):937-944. PMID 28116536
46. Taradaj J, Halski T, Kucharzewski M, et al. Effect of laser irradiation at different wavelengths (940, 808, and 658 nm) on pressure ulcer healing: results from a clinical study. *Evid Based Complement Alternat Med* 2013;2013:960240. PMID
47. Lucas C, van Gemert MJ, de Haan RJ. Efficacy of low-level laser therapy in the management of stage III decubitus ulcers: a prospective, observer-blinded multicentre randomised clinical trial. *Lasers Med Sci.* 2003;18(2):72-77. PMID 12928815
48. Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. *Phys Ther.* Sep 1994;74(9):812-823; discussion 824-815. PMID 8066108
49. Taly AB, Sivaraman Nair KP, Murali T, et al. Efficacy of multiwavelength light therapy in the treatment of pressure ulcers in subjects with disorders of the spinal cord: A randomized double-blind controlled trial. *Arch Phys Med Rehabil.* Oct 2004;85(10):1657-1661. PMID 15468027

50. Smoot B, Chiavola-Larson L, Lee J, et al. Effect of low-level laser therapy on pain and swelling in women with breast cancer-related lymphedema: a systematic review and meta-analysis. *J Cancer Surviv.* Jun 2015;9(2):287-304. PMID 25432632
51. Omar MT, Shaheen AA, Zafar H. A systematic review of the effect of low-level laser therapy in the management of breast cancer-related lymphedema. *Support Care Cancer.* Aug 9 2012;20:2977-2984. PMID 22875413
52. Omar MTA, Ebid AA, El Morsy AM. Treatment of post-mastectomy lymphedema with laser therapy: double blind placebo control randomized study. *J Surg Res.* Jan 2011;165(1):82-90. PMID 20538293
53. Sung L, Robinson P, Treister N, et al. Guideline for the prevention of oral and oropharyngeal mucositis in children receiving treatment for cancer or undergoing haematopoietic stem cell transplantation. *BMJ Support Palliat Care.* Mar 2017;7(1):7-16. PMID 25818385
54. Carcia CR, Martin RL, Houck J, et al. Achilles pain, stiffness, and muscle power deficits: achilles tendinitis. *J Orthop Sports Phys Ther.* Sep 2010;40(9):A1-26. PMID 20805627
55. News Now Staff. Laser Therapy a Slight Winner in Analysis of Electrotherapy Modalities for Adhesive Capsulitis *PT in Motion News* 2014; http://www.apta.org/PTinMotion/News/2014/10/3/LaserTherapyCapsulitis/. Accessed May 25, 2018.
56. National Institute for Health and Care Excellence (NICE). Low back pain in adults: early management [CG88]. 2009; https://www.nice.org.uk/guidance/CG88. Accessed May 24, 2018.
57. National Institute for Health and Care Excellence (NICE). Low back pain and sciatica in over 16s: assessment and management [NG59]. 2016; https://www.nice.org.uk/guidance/NG59/chapter/Recommendations. Accessed May 24, 2018.
58. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med.* Oct 2 2007;147(7):478-491. PMID 17909209
59. Chou R, Loeser JD, Owens DK, et al. Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: an evidence-based clinical practice guideline from the American Pain Society. *Spine (Phila Pa 1976).* May 1 2009;34(10):1066-1077. PMID 19363457
60. Qaseem A, Wilt TJ, McLean RM, et al. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* Apr 4 2017;166(7):514-530. PMID 28192789
61. American Academy of Orthopaedic Surgeons. Management of Carpal Tunnel Syndrome: Evidence-Based Clinical Guideline. 2016; https://www.aaos.org/uploadedFiles/PreProduction/Quality/Guidelines_and_Reviews/guidelines/CTS%20CPG_6%207%202016.pdf. Accessed May 24, 2018.
62. Blue Cross Blue Shield Association. Medical Policy Reference Manual, No. 2.01.56 (June 2019).

Documentation for Clinical Review

Please provide the following documentation (if/when requested):

- History and physical and/or consultation notes including:
  - Reason for low-level laser therapy
  - Cancer treatment (if applicable)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms

of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

MN/IE
The following services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

Type	Code	Description
CPT®	97026	Application of a modality to 1 or more areas; infrared
HCPCS	S8948	Application of a modality (requiring constant provider attendance) to one or more areas; low-level laser; each 15 minutes
ICD-10 Procedure	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action	Reason
03/01/2006	Medical Policy Committee adopted CTAF technology recommendation. New Policy.	Medical Policy Committee
07/15/2009	Code revision	Administrative Review
07/22/2009	Administrative update	Administrative Review
10/01/2010	Policy Revision with title change from Low-Level Laser Therapy for the Treatment of Carpal Tunnel Syndrome	Medical Policy Committee
05/29/2015	Coding update	Administrative Review
09/30/2015	Policy revision with position change	Medical Policy Committee
04/01/2016	Policy revision with position change	Medical Policy Committee
04/01/2017	Policy revision without position change	Medical Policy Committee
08/01/2018	Policy revision without position change	Medical Policy Committee
09/01/2019	Policy revision without position change	Medical Policy Committee

Definitions of Decision Determinations

Medically Necessary: A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.