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Research

Photobiomodulation therapy does not decrease pain and disability in people with non-specific low back pain: a systematic review

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KEY WORDS

Low-level laser therapy
Light emitting diode therapy
Phototherapy
Musculoskeletal disorders
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ABSTRACT

Question: In people with non-specific low back pain (LBP), what are the effects of photobiomodulation therapy (PBMT) on pain, disability and other outcomes when compared with no intervention, sham PBMT and other treatments, and when used as an adjunct to other treatments? **Design**: Systematic review of randomised trials with meta-analysis. **Participants**: People with acute/subacute or chronic non-specific LBP. **Interventions**: Any type of PBMT (laser class I, II and III and light-emitting diodes) compared with no treatment, sham PBMT and other types of treatment, or used as an adjunct to another treatment. **Outcome measures**: Pain intensity, disability, overall improvement, quality of life, work absence and adverse effects. **Results**: Twelve randomised controlled trials were included (pooled n = 1,046). Most trials had low risk of bias. Compared with sham PBMT, the effect of PBMT on pain and disability was clinically unimportant in people with acute/subacute or chronic LBP. In people with chronic LBP, there was no clinically important difference between the effect of PBMT and the effect of exercise on pain or disability. Although benefits were observed on some other outcomes, these estimates were imprecise and/or based on low-quality evidence. PBMT was estimated to reduce pain (MD −11.20, 95% CI −20.92 to −1.48) and disability (MD −11.90, 95% CI −17.37 to −6.43) more than ultrasound, but these confidence intervals showed important uncertainty about whether the differences in effect were worthwhile or trivial. Conversely, PBMT was estimated to reduce pain (MD 19.00, 95% CI 9.49 to 28.51) and disability (MD 17.40, 95% CI 8.60 to 26.20) less than Tecar (Energy Transfer Capacitive and Resistive) therapy, with marginal uncertainty that these differences in effect were worthwhile. **Conclusion**: Current evidence does not support the use of PBMT to decrease pain and disability in people with non-specific LBP. **Registration**: CRD42018088242. **[Tomazoni SS, Almeida MO, Bjordal JM, Stausholm MB, Machado CSM, Leal-Junior ECP, Costa LOP (2020) Photobiomodulation therapy does not decrease pain and disability in people with non-specific low back pain: a systematic review. *Journal of Physiotherapy* 66:155–165]**

Introduction

Low back pain (LBP) is a highly prevalent condition worldwide[1,2] and the leading cause of years lived with disability.[3] In most cases, the specific pathological cause remains unidentified; therefore, the term non-specific LBP is commonly used for such cases.[4] Many non-pharmacological therapies are available for the treatment of LBP, which aim to reduce pain and disability.[1] Among these options, photobiomodulation therapy (PBMT) has been recently recommended by the American College of Physicians clinical practice guidelines for the treatment of LBP.[5] However, the strength of this recommendation was supported by only three existing randomised controlled trials.[6–8]

A new terminology established in 2015 defined PBMT as a non-thermal and non-ionising light therapy applied in the form of light amplification by the stimulated emission of radiation (laser), light-emitting diodes (LEDs), and/or broadband irradiation in the visible and infrared spectra.[9] PBMT acts through the interaction between the light emitted and photoreceptors present in mitochondria in different tissues.[9,10] This interaction triggers positive effects such as stimulation of cellular metabolism and negative effects such as inhibition of cellular metabolism.[11] Various PBMT parameters can be applied but doses appear to need to be inside a therapeutic window to trigger positive effects.[12–14] A recently published editorial[15] highlighted that although there is a guideline with recommended PBMT doses for the treatment of musculoskeletal disorders and tendinopathies,[16] the

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issue of the optimal PBMT dosage remains to be addressed, which may lead to misleading conclusions.[15] Trials that presumably used inadequate PBMT doses have failed to get positive biological responses in conditions like carpal tunnel syndrome and osteoarthritis.[17,18] On the other hand, there is evidence that PBMT was effective in the treatment of several musculoskeletal disorders such as neck and shoulder pain, temporomandibular disorders and tendinopathies.[19–25] Laboratory studies have suggested that PBMT can reduce inflammation, limit tissue damage processes and promote myotube proliferation.[25]

The effectiveness of light-based therapy in people with LBP has been summarised in three systematic reviews.[26–28] The first one was published in 2008[26] when PBMT was known as low-level laser therapy. This systematic review included seven randomised trials that compared the effectiveness of PBMT against no treatment, placebo or other interventions in people with acute, subacute and chronic LBP. The authors concluded that there was insufficient data for conclusive recommendations on the clinical effects of PBMT in people with LBP. The second systematic review was published in 2015[27] and also included seven randomised trials. The third systematic review was published in 2016[28] and retrieved 15 randomised trials. The last two systematic reviews[27,28] compared light-based therapy only against placebo in people with chronic LBP. In addition, the authors claimed that they included only randomised trials investigating the effects of low-level laser therapy. However, one trial[29] was misclassified as low-level laser therapy instead of high-intensity laser therapy and was mistakenly included in both systematic reviews.[27,28] In addition, the 2016 systematic review[28] included several randomised trials investigating the effects of laser acupuncture. Thus, both reviews[27,28] do not pertain to the effects of PBMT in people with LBP because although laser acupuncture and high-intensity laser therapy are light-based therapies, neither of these is currently considered as PBMT. High-intensity laser therapy promotes thermal effects, whereas PBMT, by definition, is a non-thermal process.[9,10] In addition, laser acupuncture is the photonic stimulation of acupuncture points aiming to obtain similar effects as those obtained using acupuncture with needles, along with the added benefits of light stimulation.[30]

Recommendations about the use of PBMT in clinical practice should preferably be supported by a high-quality systematic review. The last high-quality systematic review on this topic was published in 2008 and new trials[31–35] have been conducted since then. Therefore, an updated systematic review regarding the effects of PBMT on LBP is necessary in order to provide the best available evidence to clinicians and people. It is important to summarise all the available evidence about the effects of PBMT in people with acute, subacute and chronic LBP. In addition, it is important to summarise the evidence regarding the effectiveness of PBMT compared with other types of interventions.

Therefore, this systematic review was conducted to summarise the effects of PBMT on pain and disability in people with non-specific LBP, when: compared with control conditions (such as minimal intervention, placebo and no treatment); compared with other interventions; and used as an adjunct to other treatments. Furthermore, a subgroup analysis was conducted to investigate the adequacy of PBMT dosage based on doses recommended by the World Association for Photobiomodulation Therapy (WALT).[16]

Therefore, the research question for this systematic review was:

In people with non-specific low back pain, what are the effects of photobiomodulation therapy on pain and disability when compared with control conditions, when compared with other interventions and when used as an adjunct to other treatments?

Methods

This systematic review followed the recommendations of the Cochrane Handbook of Systematic Reviews.[36]

Identification and selection of studies

Five databases were searched for eligible trials without language restriction from inception until May 2019: MEDLINE (Ovid), Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Physiotherapy Evidence Database (PEDro). Manual searches were conducted of the reference lists of prior systematic reviews on this topic and any trials included in the present review. Clinical trial records databases and grey literature (eg, congress proceedings) were also searched. The detailed search strategies are described in Appendix 1 on the eAddenda.

Two independent reviewers independently screened all titles and abstracts retrieved by the searches to identify potentially eligible trials. Any record that was judged potentially eligible by at least one of the reviewers was retrieved in full text and assessed by both reviewers against the eligibility criteria. A third reviewer resolved any disagreements.

Types of participants

The inclusion criteria for participants are presented in Box 1. Participants were not excluded by gender. Any duration of LBP was acceptable and categorised as acute/subacute ($<$ 12 weeks) or chronic ($\geq$ 12 weeks).[37] Trials that presented a mixed sample (acute/subacute and chronic together) were included only when the data were presented separately. Moreover, we excluded trials in which the participants presented LBP due to a specific pathology such as infection, inflammatory diseases, rheumatoid arthritis, nerve root compromise, fractures or neoplasms.

Types of interventions

Trials were only included if they estimated the effects of any type of PBMT (laser class I, II or III or LED), including all wavelengths. Other light-based therapy such as laser acupuncture and high-intensity laser (laser class IV) were not included because they are not PBMT.[9,10,30] The eligible comparators are listed in Box 1.

Types of outcomes measures

The primary outcomes were: pain intensity, measured by the Pain Numerical Rating scale[38] or another validated quantitative measurement method; and disability, measured by the Roland-Morris Disability Questionnaire,[39,40] Oswestry Disability Questionnaire[41] or another validated quantitative measurement method. These

Box 1. Inclusion criteria.

Design
- Randomised trial

Participants
- Age $\geq$ 18 years
- Non-specific LBP

Intervention
- PBMT (Laser Class I, II, and III and LED)

Outcome measures
- Pain intensity
- Disability
- Overall improvement or satisfaction with treatment
- Quality of life
- Work status
- Adverse events

Comparisons
- PBMT versus control (minimal intervention, sham PBMT or no intervention)
- PBMT with another intervention versus the same intervention
- PBMT versus another active intervention

LBP = low back pain, LED = light-emitting diode, PBMT = photobiomodulation therapy.

outcomes reflect the most recent core outcome set for people with LBP.[42,43]

The secondary outcomes were: overall improvement or satisfaction with treatment, as reported by participants or therapists, or measured by the Global Perceived Effect scale[38] or other validated instruments; quality of life reported by questionnaires such as the SF-12,[44] SF-36,[45] or EuroQoL;[46] return to work, work absence, or days of reduced activities;[47] and adverse effects.

Assessment of characteristics of the studies

Two reviewers independently extracted the following data from the included trials: bibliometric data, sample size, characteristics of the participants (age, gender and duration of pain), and details of the interventions, outcome measures and results. A third reviewer resolved any disagreements. When necessary, the authors of the included trials were contacted to provide additional information or trial data. In the data extraction phase, all PBMT characteristics and dosages were checked for accuracy by recalculating them as recommended by the WALT,[48] based on the data available in the trials or through e-mail correspondence with the authors.

Risk of bias

The risk of bias in the included trials was rated using the PEDro scale, which also rates the completeness of statistical reporting.[49] The total PEDro score ranges from 0 to 10, calculated by summing the number of criteria achieved with the exception of criterion 1, which is not considered in the final score.[49] Two independent reviewers evaluated any included trial with the PEDro scale, unless a score was already provided on the PEDro webpage (then this score was selected). The trials were considered as 'low risk' of bias if they had a score of ≥ 6 points. Trials with scores < 6 points were considered as having 'high risk' of bias.[50]

Data analysis

Measures of treatment effect

The effects of the interventions on (sub)acute and chronic LBP were analysed separately. Data were calculated in relation to the short term (outcomes assessed closest to 4 weeks after randomisation), medium term (outcomes assessed closest to 6 months after randomisation) and long term (outcomes assessed closest to 1 year after randomisation).[51] Results from an intention-to-treat analysis approach were used whenever possible.

All continuous outcome data were converted to a common scale ranging from 0 to 100 and synthesised using the mean difference (MD) method with its respective 95% confidence intervals. The standard deviations for analysis were extracted or if necessary estimated from other variance data using the methods described in the Cochrane Handbook.[36] Categorical outcomes data were reported as relative risk (RR) with 95% confidence interval. All possible meta-analyses were conducted using systematic review software[a]. When there were trials with sufficient homogeneity in the comparison, a meta-analysis was performed using the random effects model to calculate the pooled treatment effect with the 95% confidence interval.

The size of treatment effects were categorised as: small (ie, MD $<$ 10% of the scale; RR > 0.8 or < 1.25), moderate (MD 10 to 20% of the scale; RR 1.25 to 2.0, or 0.5 to 0.8) or large (MD $>$ 20% of the scale, RR > 2.0 or < 0.5).[52] The effect was considered clinically important when the effect size was at least moderate.[53,54]

Dealing with missing data

Missing standard deviations were calculated based on *t*-values and *p*-values for differences in means.[36] When only the mean and standard deviation of changes from baseline were reported, these values were used in the analysis.

Assessment of heterogeneity

The presence of between-trial statistical heterogeneity was assessed using the I^2 statistic. The quality of evidence was downgraded for inconsistency if considerable between-group statistical heterogeneity ($I^2 > 50\%$) was detected.

Data synthesis

The overall quality of the evidence for each outcome was evaluated using the Grading of Recommendations, Development and Evaluation (GRADE) system,[36] regardless of whether there was sufficient information to summarise the data in a quantitative analysis. The following five factors were considered for classifying the quality of the evidence, where for each factor not met, the quality of evidence was reduced by one level (from high to moderate, low or very low):[36,55] risk of bias ($>$ 25% of the trials included in the comparison were classified as high risk of bias); inconsistency ($I^2 > 50\%$): indirectness ($>$ 50% of the participants were not related to the trial's target audience); imprecision ($<$ 400 participants in the comparison for continuous outcomes and $>$ 300 participants for categorical outcomes); and publication bias (evaluated using a funnel plot when $>$ 10 trials in the same comparison). Single trial comparisons ($<$ 400 participants for continuous outcomes and $<$ 300 participants for dichotomous outcomes) were considered to be inconsistent and imprecise, providing 'low-quality evidence', which could be downgraded to 'very low-quality evidence' if limitations were identified regarding risk of bias.[52,54]

The quality of the evidence was categorised as follows. Evidence was high quality if the results were consistent in $\geq$ 75% of the participants, with low risk of bias, without publication bias, and with consistent, direct, and precise data; further research is unlikely to change the estimate or confidence in such results. Evidence was moderate quality when one of the five classification factors above was not met; further research is likely to change the estimated effect and impact confidence in the effect. Evidence was low quality when two of the five classification factors were not met; future research is likely to change the estimated effect and will have a significant impact on confidence in the effect. Evidence was very low quality when three of the five classification factors were not met; any estimate of effect is very uncertain.

Subgroup analysis

We performed the subgroup analysis for adequacy of PBMT dosage based on the dosages recommended by WALT.[16] WALT recommends irradiating the lumbar spine with the following doses: $\geq$ 4 joules per treatment point (4 to 8 points or cm^2) using 780 to 860 nm laser and $\geq$ 1 joules per treatment point (4 points or cm^2) using 904 nm laser.[16] According to these recommendations the included trials were divided into two subgroups: assumed adequate dose or assumed inadequate dose (not mentioned in guidelines or low dose).

Sensitivity analysis

When enough data were available, sensitivity analyses were conducted to assess the influence of trials with high risk of bias and unpublished trials on the estimated effect of treatment for primary outcomes.[56]

Results

Flow of studies through the review

The initial electronic database search identified a total of 1,977 records, of which 40 appeared potentially eligible after screening by title and abstract. Assessment of full text identified 12 eligible trials[6–8,31–35,57–60] (pooled n = 1,046), among which 10 trials[6–8,31–33,35,57–59] provided data that were amenable to meta-analysis (pooled n = 680). The flow diagram of the full selection process and the inclusion of trials is presented in Figure 1. Articles excluded by full-text evaluation are presented with the reasons for exclusion in Table 2 on the eAddenda.

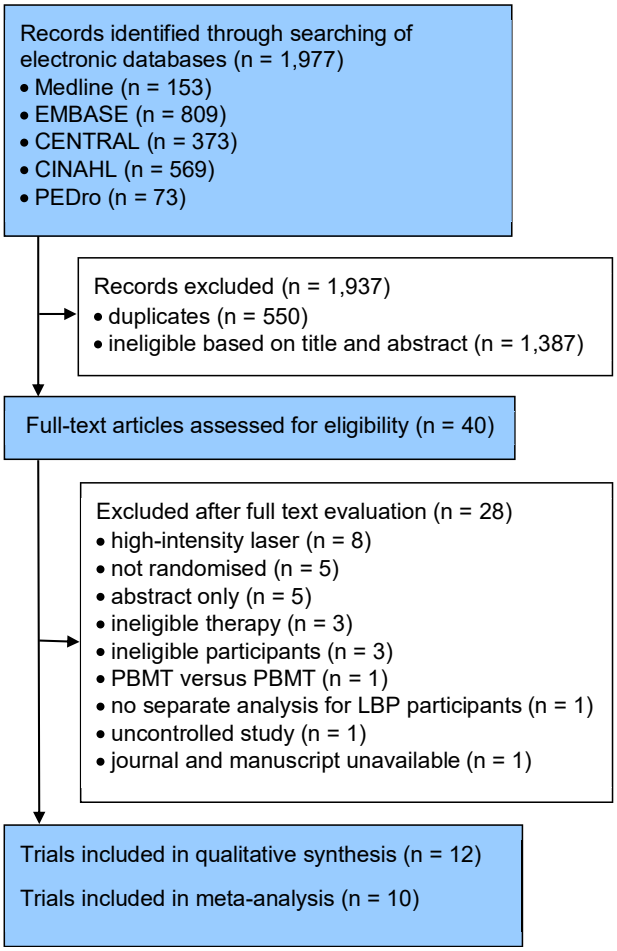

Figure 1. Flow of trials through the review.
PBMT = photobiomodulation therapy, LBP = low back pain.

Characteristics of the included studies

Risk of bias

The results of risk of bias assessment are presented in Table 1. The PEDro score of the included trials ranged from 2 to 9 points (mean 6.6 points, SD 1.8). Random allocation was applied in every trial. However, 75% and 67% of the trials did not performed intention-to-treat analysis and concealed allocation, respectively. Moreover, the therapists and participants were not blinded in 58% and 50% of the trials, respectively. In contrast, the assessors were blinded in 83% of the trials. The baseline scores were similar in 83% of the trials, follow-up was adequate in 67% of the trials, between-group comparisons were reported in 92% of the trials and a point measure and measure of variability were reported in 83% of the trials. Nine trials were considered as having a low risk of bias[6–8,31–33,35,57,59] and three trials were considered as having a high risk of bias.[34,58,60]

Participants

The participants had acute LBP in two trials[31,60] and chronic LBP in 11 trials[6–8,31–35,57–59] (range 7 months to 110 months, based on six trials). One trial[31] included a mixed sample (acute and chronic) and the data were presented separately. One trial[60] included people with acute LBP, although the duration of symptoms was not explicitly reported. One trial[8] included people with LBP for a duration of $\geq$ 4 weeks; however, the mean duration of symptoms was $>$ 3 months (ie, most had chronic LBP: 7 months in the PBMT group and 13 months in the control group) and thus the trial was included in the meta-analysis of chronic LBP. The duration of pain in another two trials was not reported; however, the authors claimed that all the participants had chronic LBP.[6,33]

Interventions

Detailed description of the included trials' characteristics can be found in Table 3. The source of PBMT, parameters used, and frequency and duration of treatment varied substantially among the trials. Detailed specifications of the PBMT interventions are presented in Table 4 on the eAddenda.

Low-level laser therapy was applied in most trials.[6,7,31,33–35,57–60] One trial[8] used a 1,060 nm Nd-Yag laser and another trial[32] used a pad of LEDs. The light was applied in a steady mode with direct skin contact in 10 trials.[6–8,31,32,35,57–60] One trial[34] used scanning mode, while another trial[33] used a combination of steady mode with direct skin contact on the spine and scanning mode on paravertebral muscles.

All energy doses (J) were recalculated (even when provided by authors) for each trial included and ranged from 0.06 to 31.2 J per point (Table 4 on the eAddenda). In seven trials,[7,8,31,32,57,59,60] the full description of parameters (eg, treatment time, spot size and average power) were not stated explicitly and so were calculated based on the available information.

Only four trials[31,35,57,58] used the recommended and assumed adequate doses according to WALT recommendations.[16] A wavelength that was not mentioned in the guidelines was used in one trial,[8] while another trial[32] used LED (also not mentioned in WALT recommendations), and were thus assumed to have an inadequate dose. Moreover, one trial[59] was assumed to have an inadequate dose due a low dose applied per point. Two trials[33,34] were allocated to the assumed inadequate dose subgroup due to the scanning mode that was used. In scanning mode it is not possible to estimate the total dose delivered, and therefore its adequacy. Moreover, three trials[6,7,60]

Table 1
PEDro scores of included trials.[61]

Trial	Eligibility and source[a]	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	< 15% dropouts	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total (0 to 10)
Ay[31]	N	Y	N	Y	Y	N	Y	Y	N	Y	Y	7
Basford[8]	Y	Y	N	Y	Y	Y	Y	Y	N	Y	N	7
Djavid[57]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Gur[58]	Y	Y	N	Y	N	N	Y	N	N	Y	Y	5
Hsieh[32]	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9
Klein[59]	Y	Y	N	Y	Y	Y	Y	N	N	Y	Y	7
Longo[60]	N	Y	N	N	N	Y	N	N	N	N	N	2
Nambi[33]	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y	7
Notarnicola[34]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Soriano[7]	N	Y	N	Y	Y	Y	Y	N	N	Y	Y	7
Tantawy[35]	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Toya[6]	N	Y	Y	N	Y	Y	Y	Y	N	Y	Y	8

N = no, Y = yes.
[a] Relates to external validity and therefore does not contribute to the total score.

Table 3
Characteristics of included trials.

Study	Participants	Interventions[a]	Outcome measures[b]
Ay[31]	n = 80 Age *(yr)* = NS Pain duration = NS	Exp = PBMT and hot pack Con = Sham PBMT and hot pack	• Pain • Disability • Overall improvement • Adverse event After treatment[c], not further specified
Basford[8]	n = 59 Age *(yr)* = 18 to 70 Pain duration *(mth)* > 1	Exp = PBMT Con = Sham PBMT	• Pain • Overall improvement • Adverse events End-treatment (Week 4)[c] and 4 to 5 wk later
Djavid[57]	n = 61 Age *(yr)* = 20 to 60 Pain duration *(mth)* ≥ 3	Gr 1 = PBMT and exercise (strengthening, stretching, mobilising, co-ordination and stabilising of the abdominal, back, pelvic and lower limb muscles, dependent on the clinical findings) Gr 2 = Sham PBMT and exercise (as above) Gr 3 = PBMT	• Pain • Disability • Adverse event End-treatment (Week 6)[c] and Week 12
Gur[58]	n = 75 Age *(yr)* = 20 to 50 Pain duration *(mth)* ≥ 12	Gr 1 = PBMT and exercise (lumbar flexion and extension, knee flexion, hip adduction, and strengthening exercises Gr 2 = Exercise (as above) Gr 3 = PBMT	• Pain • Disability End-treatment (Week 4)[c]
Hsieh[32]	n = 70 Age *(yr)* = 18 to 65 Pain duration *(mth)* > 3	Exp = PBMT Con = Sham PBMT	• Pain • Disability • Quality of life • Adverse events End-treatment (Week 2)[c]
Klein[59]	n = 20 Age *(yr)* = 21 to 55 Pain duration *(mth)* ≥ 12	Exp = PBMT and exercise (flexion and extension exercises) Con = Sham PBMT and exercise (as above)	• Pain • Disability • Adverse events End-treatment (Week 4)[c] and monthly for 6 mth
Longo[60]	n = 120 Age *(yr)* = 40 to 65 Pain duration = 'acute', not further defined	Gr 1 = PBMT Gr 2 = Sham PBMT Gr 3 = Laser CO_2 (wavelength = 10,600 nm; treatment time/cm^2 = 3 s; power density/diode = 1 W/cm^2; paravertebral region and possible trigger points)	• Overall improvement After 3 and 5 applications, and Months 1[c]
Nambi[33]	n = 330 Age *(yr)* > 18 Pain duration *(mth)* ≥ 3	Gr 1 = PBMT and exercise (strengthening of the abdominal and back muscles) Gr 2 = Exercise (as above) Gr 3 = PBMT, exercise (as above) and spinal manipulation of L4–L5 segment	• Pain • Disability • Quality of life • Adverse events End-treatment (Week 4)[c] and Months 6[c] and 12[c]
Notarnicola[34]	n = 60 Age *(yr)* ≥ 18 Pain duration *(mth)* ≥ 3	Exp = PBMT Con = Tecar therapy (10 min of capacitive phase (600 kHz) and 10 min of resistive phase (450 kHz) of Tecar therapy (each session); the power of energy in both phases was the same: 10 to 12 VA, equivalent to 0.42 J/cm^2, area of 28.2 cm^2)	• Pain • Disability • Adverse events End-treatment (Week 2) and Weeks 6[c] and 10
Soriano[7]	n = 85 Age *(yr)* > 60 Pain duration *(mth)* > 3	Exp = PBMT Con = Sham PBMT	• Pain End-treatment (Week 2)[c]
Tantawy[35]	n = 45 Age *(yr)* = 30 to 40 Pain duration *(mth)* = 3	Gr 1 = PBMT and exercise (strengthening, stretching, mobilisation, coordination, and maintaining stabilisation of the back, abdominal, pelvic and lower extremity muscles) Gr 2 = Exercise (as above) Gr 3 = Exercise (as above) and ultrasound (1 MHz; intensity = 1 W/cm^2; time = 10 min; one probe; effective radiating area = 5 cm^2; lumbar vertebral region; 2/wk × 8 wk = 16 sessions)	• Pain • Disability End-treatment (Week 8)[c]
Toya[6]	n = 41 Age *(yr)* = NS Pain duration = NS	Exp = PBMT Con = Sham PBMT	• Pain End-treatment (Day 0)[c] and Day 1

Con = control group, Exp = experimental group, Gr = group, PBMT = photobiomodulation therapy.
[a] Details of the PBMT used in each trial are presented in Table 4 on the eAddenda.
[b] Only the outcomes relevant to this review are listed.
[c] Time points considered in this systematic review.

could not be allocated in either subgroup due a lack of information (eg, treatment time, energy and number of treated points). It was not possible to calculate the total dose in these trials and was thus assumed to have an unclear dose.

The frequency of PBMT treatment ranged from two to five times per week. A single session was undertaken in one trial.[6] Excluding one trial,[6] the number of sessions ranged from six to 20, but most of them were > 10 or 12 sessions in total.

Comparisons

In one trial, PBMT plus hot packs was compared with placebo plus hot packs.[31] In four trials, PBMT was compared with sham PBMT.[6–8,32] In one trial, PBMT was compared with Tecar therapy (Energy Transfer Capacitive and Resistive), which is a technological evolution of diathermy.[34] One trial[57] was a three-arm trial comparing PBMT with PBMT plus exercise and with sham PBMT plus exercise. In another three-arm trial,[58] PBMT was compared with PBMT plus exercise and

with exercise alone. In one trial[59] there was a comparison of PBMT plus exercise and sham BPMT plus exercise. In another three-arm trial,[33] the interventions that were compared were exercise, PBMT plus exercise, and PBMT plus spinal manipulation plus exercise. In a three-arm trial[35] there was a comparison of PBMT plus exercise, exercise and ultrasound plus exercise. The exercise programs in these trials were considered to be comparable. Finally, in one trial[60] with three arms there was a comparison of PBMT, placebo and high-intensity laser (CO_2 laser, 10,600 nm).

Outcome measures

Eleven trials[6–8,31–35,57–59] measured pain intensity. Only two of them[6,7] did not present the results using continuous data. One of these trials[7] reported the results as the percentage of pain relief, categorised as poor, regular, good or excellent, and the treatment was considered effective when the response was good or excellent. In another trial[6] pain was dichotomised as excellent, good or fair improvement versus little or no change or exacerbation. Various instruments were used to measure disability: Roland Morris Disability Questionnaire, Oswestry Disability Index and Modified Oswestry Disability Index. Measurement of secondary outcomes was not frequent among trials. Nine trials[6–8,31–34,57,59] reported no adverse effects. The time-points of assessments of patients ranged from immediately after the end of one single treatment session[6] to 1 year after baseline.[33] The outcome measures and measuring instruments are presented in Table 5 on the eAddenda.

Effects of interventions

The effects on the primary outcomes for each comparison are presented below, separated by whether the participants had acute/subacute or chronic LBP. The effects on the secondary outcomes for each comparison are presented in Appendix 2 on the eAddenda.

PBMT versus sham PBMT for acute/subacute LBP

Pain intensity

One trial with low risk of bias[31] (assumed adequate dose) compared PBMT plus hot packs with sham PBMT plus hot packs on acute LBP. It provided low-quality evidence (downgraded due to inconsistency and imprecision) that PBMT is unlikely to provide a worthwhile benefit on pain intensity at short-term follow-up (MD 7.00, 95% CI −1.87 to 15.87, n = 40).

Disability

One trial with low risk of bias[31] measured disability. It provided low-quality evidence (downgraded due to inconsistency and imprecision) that PBMT did not have a worthwhile effect on disability at short-term follow-up (MD −1.00, 95% CI −11.06 to 9.06, n = 40).

PBMT versus other treatments for acute/subacute LBP

The trial comparing PBMT with CO_2 laser for acute/subacute LBP is presented in Appendix 2 on the eAddenda.

PBMT versus sham PBMT for chronic LBP

Pain intensity

Four trials with low risk of bias[6–8,32] compared PBMT versus sham PBMT at short-term follow-up (closest to 4 weeks). Moreover, three trials with low risk of bias compared PBMT with sham PBMT associated with either hot packs[31] or exercise[57,59] also at short-term follow-up (closest to 4 weeks).

Five trials[8,31,32,57,59] measured pain intensity using continuous scales, while two trials[6,7] measured pain intensity using categorical scales. Thus, these trials were separated into two meta-analyses (continuous and dichotomous) to estimate the effectiveness of PBMT compared with sham PBMT at short-term follow-up.

Included in the first meta-analysis were five trials[8,31,32,57,59] that used a visual analogue scale to measure pain intensity, with low risk of bias. They provided low-quality evidence (downgraded due to inconsistency and imprecision) that PBMT did not have a worthwhile effect on pain at short-term follow-up (MD −3.95, 95% CI −10.98 to 3.08, n = 230). See Figure 2a, or for a detailed forest plot see Figure 3a on the eAddenda.

One trial[7] measured pain with a visual analogue scale but reported the results as percentage of relief. Pain was considered improved when the pain relief evaluation was 60 to 100%. Thus, in this systematic review, we transformed the pain intensity data from this trial[7] at short-term into a categorical outcome (improved or not). Furthermore, investigators of another trial[6] also measured pain with their own scale and provided the results as categorical data. Pain was considered improved when graded as excellent, good or fair, but not when it was graded as little or no change and exacerbated. These two trials[6,7] with low risk of bias and an unclear dose provided low-quality evidence (downgraded due to inconsistency and imprecision) that the effect of PBMT on pain intensity at short-term follow-up remains very uncertain (RR 0.32, 95% CI 0.08 to 1.34, n = 126). See Figure 2b, or for a detailed forest plot see Figure 3b on the eAddenda.

Disability

Five trials[8,31,32,57,59] with low risk of bias were meta-analysed to estimate the effect on disability in the short term. The meta-analysis provides low-quality evidence (downgraded due to inconsistency and imprecision) that any effect of PBMT is too small to be worthwhile (MD −4.83, 95% CI −10.29 to 0.64, n = 230). See Figure 2c, or for a detailed forest plot see Figure 3c on the eAddenda.

Subgroup analysis

Subgroup analyses were performed of the two trials with assumed adequate dose of PBMT[31,57] and three trials with assumed inadequate dose.[8,32,59] See Figure 2a, c and d, or for more detail see Figure 3a, c and d on the eAddenda. The pooled effect size showed that PBMT is unlikely to have a worthwhile effect on pain intensity at short-term follow-up both for assumed adequate dose (MD −2.57, 95% CI −9.67 to 4.54, n = 81) and assumed inadequate dose (MD −5.28, 95% CI −18.05 to 7.49, n = 149). Furthermore, the pooled effect size also indicates that PBMT is unlikely to have a worthwhile effect on disability at short-term follow-up both for assumed adequate dose (MD −5.48, 95% CI −12.17 to 1.21, n = 81) and for assumed inadequate dose (MD −4.92, 95% CI −13.31 to 3.46, n = 149). Therefore, inclusion of only trials with adequate dosage does not appear to change the effect of PBMT compared with sham.

Effect of PBMT versus exercise for chronic LBP

Pain intensity

One trial with low risk of bias[57] and one with high risk of bias[58] were meta-analysed to estimate the effect of PBMT versus exercise. Both trials measured pain intensity at short-term follow-up to provide very low-quality evidence (downgraded due to risk of bias, inconsistency and imprecision). The estimate of the between-group difference was very imprecise (MD −2.10, 95% CI −18.71 to 14.52, n = 90). See Figure 4a, or for a detailed forest plot see Figure 5a on the eAddenda.

Disability

The same two trials[57,58] measured disability at short-term follow-up and the meta-analysis showed that there was low-quality evidence (downgraded due to risk of bias and imprecision) that PBMT does not have any worthwhile benefit over exercise (MD 4.38, 95% CI −1.39 to 10.15, n = 90). See Figure 4b, or for a detailed forest plot see Figure 5b on the eAddenda.

Effect of PBMT versus other treatments for chronic LBP

The trial[34] comparing PBMT with Tecar therapy and the trial[35] comparing PBMT with ultrasound plus exercise for chronic LBP are presented in Appendix 2 on the eAddenda.

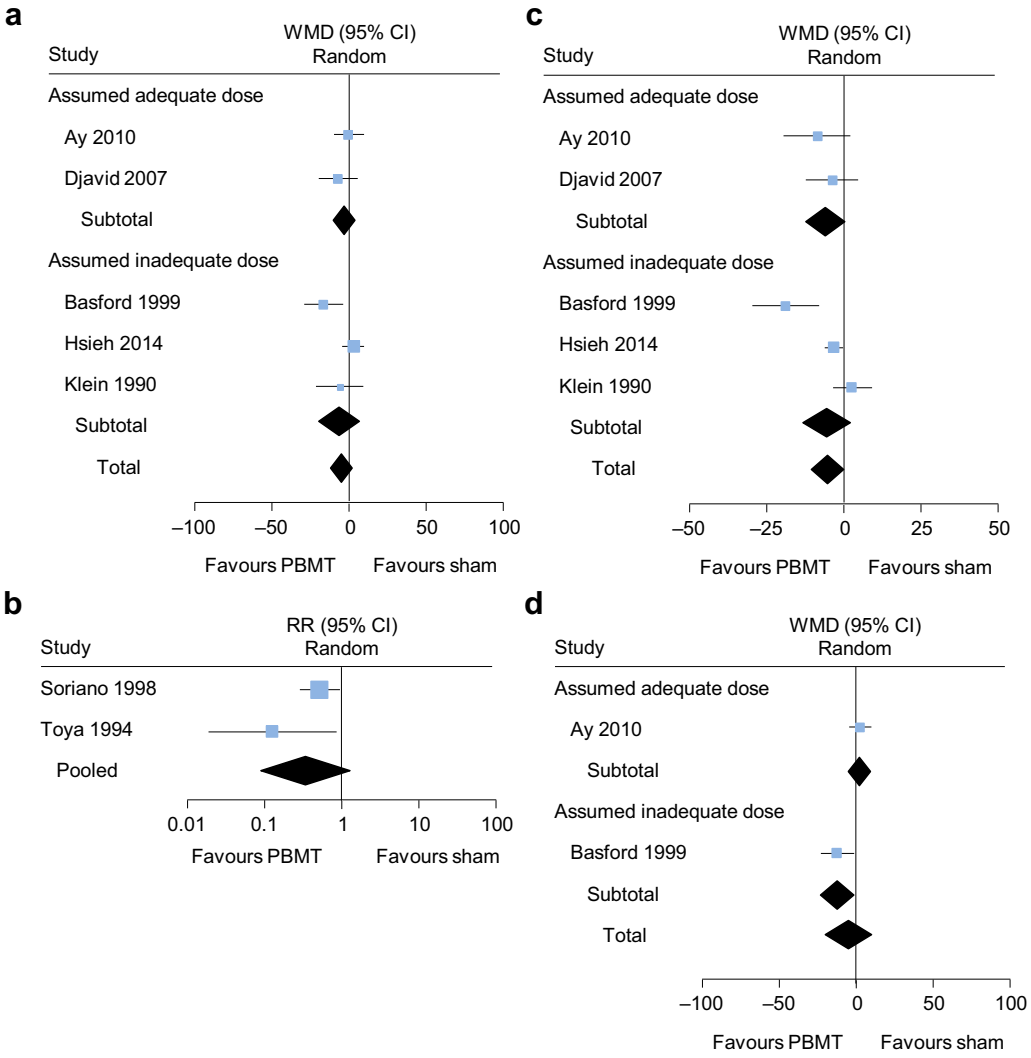

Figure 2. Meta-analysis of trials comparing photobiomodulation therapy (PBMT) with sham PBMT in chronic low back pain at short-term: (a) pain intensity (continuous outcome), (b) pain intensity (dichotomous outcome), (c) disability and (d) overall improvement.
PBMT = photobiomodulation therapy.

Effect of PBMT plus exercise versus exercise for chronic LBP

Pain intensity

One trial with high risk of bias[58] and two trials with low risk of bias[33,35] were included in the meta-analysis of the comparison of PBMT plus exercise versus exercise. These three trials measured pain intensity at short-term follow-up. They provided very low-quality evidence (downgraded due to risk of bias, inconsistency and imprecision) that the estimate of the between-group difference was very imprecise (MD −11.70, 95% CI −24.99 to 1.59, n = 300) See Figure 6a, or for a detailed forest plot see Figure 7a on the eAddenda.

One trial with low risk of bias[33] compared PBMT plus exercise with exercise in the intermediate and long term. This constituted low quality of evidence (downgraded due to inconsistency and imprecision). There was a small and clinically unimportant effect of PBMT plus exercise over exercise alone in decreased pain intensity in the intermediate term (MD −3.00, 95% CI −5.33 to −0.67, n = 110) and long term (MD −9.00, 95% CI −11.35 to −6.65, n = 110) compared with exercise alone.

Disability

The same three trials that measured pain[33,35,58] also measured disability in the short term. The meta-analysis constituted very low-quality evidence (downgraded due to risk of bias, inconsistency and imprecision). Due to the wide CI, the effect of exercise as an adjunct to exercise remained uncertain (MD −5.26, 95% CI −17.50 to 6.98, n = 300). See Figure 6b, or for a detailed forest plot see Figure 7b on the eAddenda.

One trial[33] compared PBMT plus exercise versus exercise in the intermediate and long term. There was low-quality evidence (downgraded due to inconsistency and imprecision) that there was a small and clinically unimportant effect of PBMT as an adjunct to exercise on pain intensity in the intermediate term (MD −3.00, 95% CI −5.33 to −0.67, n = 110) and long term (MD −9.00, 95% CI −11.35 to −6.65, n = 110).

Subgroup analysis

Subgroups were analysed to distinguish the two trials[35,58] with assumed adequate dose of PBMT from the trial[33] with an assumed inadequate dose. The pooled estimate of the two trials (one with high[58] and one with low[35] risk of bias) was that adequate-dose PBMT used as an adjunct to exercise decreased pain in the short term); unfortunately, this estimate had enough uncertainty to make it unclear whether the effect was clinically worthwhile or trivial (MD −18.92, 95% CI −36.44 to −1.41, n = 80). See Figure 6a, or for more detail see Figure 7a on the eAddenda. In contrast, the pooled effect size was not statistically significant for disability in the short term for either subgroup. See Figure 6b, or for more detail see Figure 7b on the eAddenda.

Effect of PBMT plus spinal manipulation plus exercise versus exercise for chronic LBP

The comparison PBMT plus spinal manipulation plus exercise versus exercise for chronic LBP[33] is presented in Appendix 2 on the eAddenda.

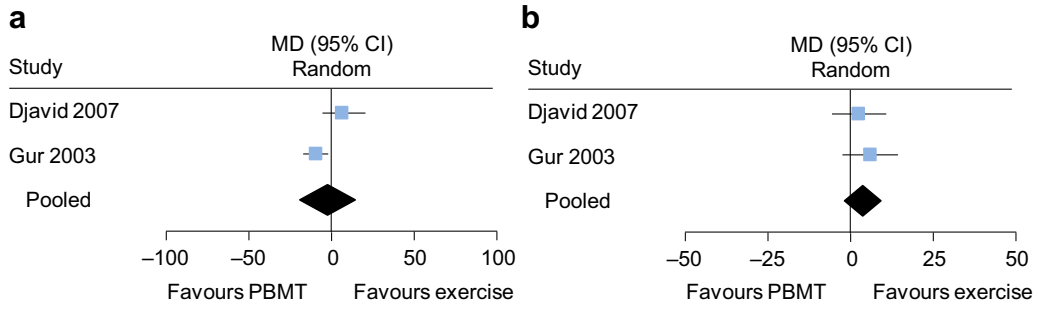

Figure 4. Meta-analysis of trials comparing photobiomodulation therapy (PBMT) with exercise in chronic low back pain at short-term: (a) pain intensity and (b) disability.
PBMT = photobiomodulation therapy.

GRADE summaries

The overall quality of evidence for each outcome in each comparison can be seen in Table 6 on the eAddenda.

Sensitivity analysis

The risk of publication bias was not assessed with funnel plots because the power of the test was too low with < 10 trials.[36] The low number of included trials also precluded a valid analysis of the impact from within-study risk of bias.

Discussion

In general, the results showed that there was low-quality evidence that PBMT was not better than sham for acute/subacute or chronic LBP in the short term. Low-quality evidence suggested that PBMT plus exercise improved pain and disability more than ultrasound plus exercise, but the 95% CI showed uncertainty about whether this effect was clinically worthwhile. Low-quality evidence also suggested that PBMT plus spinal manipulation and exercise was better than exercise alone to a moderate (and therefore clinically worthwhile) extent; unfortunately, it was not possible to distinguish how much (if any) of that benefit was due to PBMT, due to the uncontrolled co-intervention (spinal manipulation). There was low-quality evidence that PBMT was not better than Tecar therapy for chronic LBP in the short term.

Twelve randomised trials were included in this systematic review, and although most of them presented low risk of bias,[6–8,31–33,35,57,59] methods such as intention-to-treat, concealed allocation and blinding of participants and therapists were rarely used.[62] In addition, we detected some relevant problems that decreased the quality of evidence and thereby decreased confidence in the accuracy of results. Most of the included trials had a small sample size (mean of 32 participants per group), did not describe sample size calculation and, when described, the reported rationale was inadequate. Inconsistencies were also observed among the results of the included trials, probably due to the great heterogeneity among their PBMT parameters, duration and frequency of treatments, characteristics of participants, duration of follow-up, selection of outcome measurement instruments and methodological quality.

It is well accepted that the choice of PBMT parameters is crucial for the effectiveness of the therapy[19,25,63–65] because application of doses below and/or above the recommended range have been identified as a major factor that leads to negative outcomes.[63] Thus, for the interpretation of clinical trials, it is essential to evaluate the doses of PBMT.[19,25,63–65] However, most trials included in this review inadequately or insufficiently reported the PBMT parameters,[10] which make interpretation of the results difficult. Furthermore, the minimal information about parameters provided in at least four trials[6,7,34,60] could have led to a misleading picture, forcing caution in the data analysis and conclusions of this systematic review. The included trials presented extremely varied parameters. For example, the energy doses ranged from 0.06 to 31.2 J/point, irradiation time ranged from 1.5 to 2,400 seconds and average power output ranged from 4.2 to

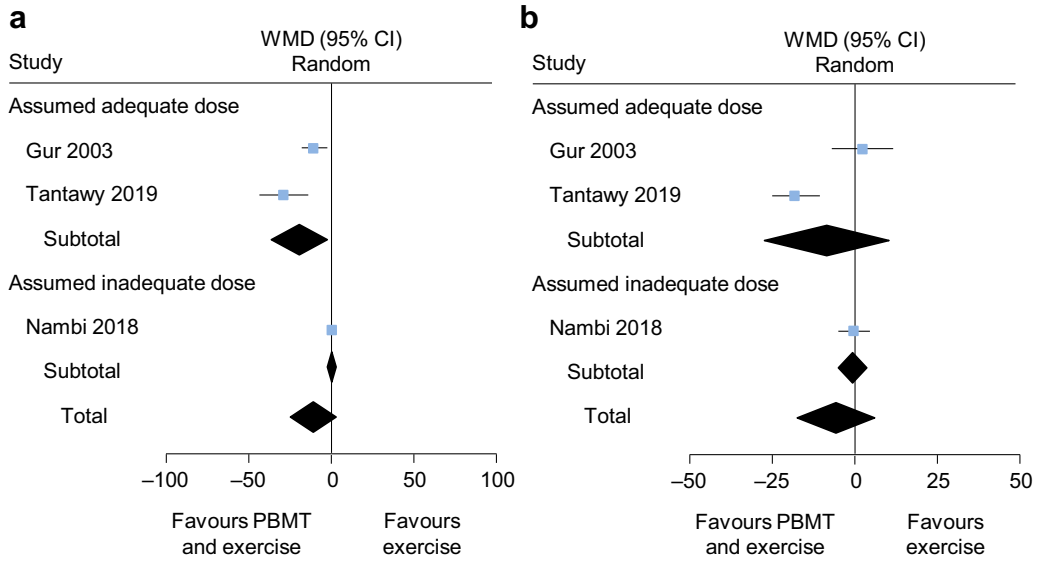

Figure 6. Meta-analysis of trials comparing photobiomodulation therapy (PBMT) plus exercise with exercise in chronic low back pain at short-term: (a) pain intensity and (b) disability.
PBMT = photobiomodulation therapy.

500 mW. Finally, these trials did not report considerations that supported the choice of parameters that were used and also did not discuss the optimisation of these parameters.

A previous systematic review[26] only qualitatively analysed the included trials and observed that PBMT, especially low-level laser therapy, was more effective than placebo, but not clinically significant, in decreasing pain intensity in the short and intermediate term in people with chronic LBP. Moreover, only one trial showed that PBMT significantly improved disability compared with placebo treatment.[8] In contrast, that same systematic review[26] concluded that PBMT was not better than exercise or exercise plus placebo treatment. Our results differ from the aforementioned systematic review, which can be explained partly by the inclusion of five new trials in our review.[31–35] In addition, we observed that data extraction was performed differently in three trials.[6,7,60] For example, Yousefi-Noraie et al[26] presented data as percentages, whereas in our review, we dichotomously presented pain intensity and overall improvement as improved or not. Moreover, the duration of follow-up considered from each included trial diverged between the systematic reviews.

Two previous systematic reviews[27,28] compared laser therapy (both low-level and high-intensity) against placebo and showed that laser therapy was effective in decreasing pain intensity in people with non-specific chronic LBP. However, it is important to highlight that although these two systematic reviews suggested that the effects of low-level laser therapy in people with chronic non-specific LBP were evaluated, one trial that evaluated the effects of high-intensity laser therapy was also included;[66] therefore, they cannot be considered as PBMT. In addition, unlike our systematic review, Glazov et al[28] included several laser acupuncture trials. Thus, we believe that the addition of a therapy different from PBMT may have positively skewed the results, explaining the divergence.

Clinical practice guidelines from the American College of Physicians recently recommended the use of PBMT for the treatment of people with chronic LBP. However, this recommendation was supported by only three randomised trials,[6–8] which observed that PBMT compared with placebo decreased pain intensity in the short term in people with chronic LBP. In contrast, our systematic review summarised 12 randomised trials and comprised all available evidence to date regarding the effects of PBMT compared with any other comparison groups in people with acute, subacute and chronic LBP. Unlike what was recommended by the American College of Physicians,[5] the present review showed that the available evidence is inadequate to support the use of PBMT in people with non-specific LBP.

In the present review, subgroup analyses investigated the adequacy of PBMT dosage, based on the doses recommended by WALT.[16] Subgroup analysis by dosage was challenging due to the limited number and reporting of studies. However, it was important to identify the limitations related to reporting of PBMT parameters in existing trials. Among the previous systematic reviews, only one performed this type of analysis.[26] Our results corroborate those reported in a study by Yousefi-Nooraie et al,[26] in which the results of subgroup analysis were the same as those of the main comparison of PBMT versus placebo. In contrast, on comparing PBMT plus exercise with exercise alone, the mean estimate of the subgroup analysis suggested that using an adequate PBMT dose had a moderate effect in decreasing pain intensity at the short-term follow-up; however, the confidence interval did not exclude the possibility that the true effect may not be clinically worthwhile. Also, it is important to highlight that one trial[58] with high risk of bias and one trial[35] with low risk of bias were included in the subgroup assumed to have received an adequate dose. Thus, these results should be interpreted with further caution because the estimates of effect may have been biased by low methodological quality.

Although WALT provides dosage guidelines, we observed that only four included trials[31,35,57,58] (33%) used the recommended and assumed adequate doses. By qualitatively analysing each of these trials (Table 7 on the eAddenda), a clinically important effect of PBMT for both the decrease in pain intensity and disability was found in only one trial.[35] In contrast, one trial[7] used an unclear dose and the mean estimate of the effect of PBMT was clinically important, although the confidence interval still included clinically unimportant effects. In addition, one trial[8] that used a wavelength (1,064 nm) that was not included in the WALT guidelines obtained a moderate and clinically important mean estimate, but again the confidence interval showed uncertainty. That study used a modified high-intensity laser device (class 4) and the observed positive outcomes might have been related to thermal sensation felt by participants. Yet, another trial[32] that used LED (also not mentioned in the WALT guidelines) showed a small and clinically unimportant effect of PBMT in decreasing disability. Thus, we observed that in trials that showed that PBMT was effective in improving the primary outcomes, the doses that were used were higher than those recommended by WALT. This suggests that increasing the PBMT dose may be beneficial in the treatment of LBP. However, problems such as small sample size, lack of concealed allocation and unblinded therapists decrease confidence in the accuracy of this suggestion.

The qualitative analysis conducted in one trial[33] showed that the association of PBMT with exercise was effective in decreasing pain intensity and disability in the intermediate and long term, but the treatment effect was small and clinically unimportant. Interestingly, the same trial showed that the combination of PBMT with spinal manipulation and exercise was effective and clinically important in decreasing pain intensity and disability in patients with chronic LBP. These results corroborate evidence showing that the combination of PBMT with exercise appears to potentiate the effects of exercise in other conditions.[10,66] However, although this trial[33] had a low risk of bias, items such as concealed allocation and blinding of participants and therapists were not used. Thus, our confidence in the accuracy of these results is low. Overall, if adequate doses of PBMT were used, better results might be observed from PBMT with exercise for LBP.

Strengths of this review included the use of a sensitive search strategy using five databases and manual searches through reference lists of manuscripts, without any publication or language restriction on data. Moreover, two independent authors conducted the screening of trials, data extraction and assessment of the methodological quality, as recommended by the Cochrane Collaboration. Finally, the quality of evidence was carefully assessed according to the GRADE approach. Unfortunately, after screening all titles and abstracts, although five congress abstracts were identified, no reply was received from the authors after contacting them via e-mail. Moreover, one trial was identified at the screening phase that contained no contact information of the authors, and neither the journal nor the manuscript were found after an extensive search. Finally, we evaluated the effects of PBMT on non-specific LBP at predetermined time points only, which potentially left some time points uncovered.

Further trials that follow rigorous methodological quality and adequate sample sizes are required to investigate the optimisation of PBMT parameters in LBP.[67] It is essential that the trials provide a rationale for the choice of parameters and/or that these parameters are optimised. In addition, the trials should investigate the optimal PBMT dosage and 'therapeutic window' for a given health condition. It is important that future trials be based on the Consolidated Standard of Reporting Trials (CONSORT) to report trials and the TIDieR checklist to increase the description of interventions.[68,69] Moreover, all PBMT parameters should be described as clearly and completely as possible, preferably as a table in the manuscript. Finally, trials that investigate the long-term follow-up are necessary because only two trials[33,60] with this characteristic were identified in this review.

Overall, there was insufficient evidence to support the use of PBMT to decrease pain intensity and disability in people with acute/subacute and chronic non-specific LBP.

What was already known on this topic: Some clinical practice guidelines have recommended photobiomodulation therapy for low back pain but with limited evidence to support this recommendation. Since the most recent systematic reviews on the topic, photobiomodulation therapy has been defined as non-thermal and non-ionising light therapy, and its effect on low back pain has been assessed in additional randomised trials.
What this study adds: Based on the available evidence from randomised trials, there is insufficient evidence to support the use of PBMT to decrease pain intensity and disability in people with acute/subacute and chronic non-specific LBP. Compared with sham, it is unlikely to have a worthwhile benefit on pain or disability, although at some time points there was insufficient data to generate a precise estimate of its effect. Although benefits were observed on some other outcomes, these estimates were imprecise and/or based on low-quality evidence.

Footnotes: [a] Review Manager Version 5.3, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark.

eAddenda: Tables 2, 4, 5, 6 and 7; Figures 3, 5 and 7; and Appendices 1 and 2 can be found online at https://doi.org/10.1016/j.jphys.2020.06.010.

Ethics approval: Not applicable.

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